

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:38:32 ; Search time 49.3333 Seconds  
(without alignments)  
3991.938 Million cell updates/sec

Title: US-09-806-194A-20  
Perfect score: 3653  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_29Jan04:\*  
1: geneseqp1980s:\*  
2: geneseqp1990s:\*  
3: geneseqp2000s:\*  
4: geneseqp2001s:\*  
5: geneseqp2002s:\*  
6: geneseqp2003as:\*  
7: geneseqp2003bs:\*  
8: geneseqp2004s:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	Score	Query		DB	ID	Description
		Match	Length			
1	3653	100.0	697	3	AAV88430	Aay88430 Human APP
2	3653	100.0	697	4	AAU07210	Aau07210 Human bet
3	3653	100.0	697	4	AAE10637	Aae10637 Human amy
4	3653	100.0	697	4	AAE06867	Aae06867 Human amy
5	3653	100.0	697	4	AAE02589	Aae02589 Human amy
6	3653	100.0	697	4	AAU06611	Aau06611 Human Amy
7	3653	100.0	697	5	ABB78598	Abb78598 Human APP
8	3646	99.8	697	3	AAV88428	Aay88428 Human APP
9	3646	99.8	697	4	AAU07208	Aau07208 Human bet

10	3646	99.8	697	4	AAE10635	Aae10635	Human	amy
11	3646	99.8	697	4	AAE06865	Aae06865	Human	amy
12	3646	99.8	697	4	AAE02587	Aae02587	Human	amy
13	3646	99.8	697	4	AAU06609	Aau06609	Human	Amy
14	3646	99.8	697	5	ABB78596	Abb78596	Human	APP
15	3643	99.7	695	2	AAW19484	Aaw19484	APP695	mu
16	3643	99.7	695	2	AAW19498	Aaw19498	APP695	mu
17	3643	99.7	695	3	AAW88436	Aay88436	Human	APP
18	3643	99.7	695	4	AAU07207	Aau07207	Human	bet
19	3643	99.7	695	4	AAE10634	Aae10634	Human	amy
20	3643	99.7	695	4	AAE06864	Aae06864	Human	amy
21	3643	99.7	695	4	AAE02586	Aae02586	Human	amy
22	3643	99.7	695	4	AAU06608	Aau06608	Human	Amy
23	3643	99.7	695	5	ABB78595	Abb78595	Human	APP
24	3641	99.7	740	7	ADB87314	Adb87314	Human	amy
25	3641	99.7	740	7	ADB87312	Adb87312	Human	amy
26	3638	99.6	697	3	AAW88429	Aay88429	Human	APP
27	3638	99.6	697	4	AAU07209	Aau07209	Human	bet
28	3638	99.6	697	4	AAE10636	Aae10636	Human	amy
29	3638	99.6	697	4	AAE06866	Aae06866	Human	amy
30	3638	99.6	697	4	AAE02588	Aae02588	Human	amy
31	3638	99.6	697	4	AAU06610	Aau06610	Human	Amy
32	3638	99.6	697	5	ABB78597	Abb78597	Human	APP
33	3636	99.5	695	1	AAP81692	Aap81692	Sequence	
34	3636	99.5	695	2	AAR26338	Aar26338	APP695.	3
35	3636	99.5	695	2	AAW19481	Aaw19481	APP695	mu
36	3636	99.5	695	2	AAW20233	Aay20233	Human	bet
37	3636	99.5	695	2	AAW07221	Aay07221	Amyloid	p
38	3636	99.5	695	3	AAW88434	Aay88434	Human	APP
39	3636	99.5	695	3	AAW44705	Aay44705	Human	bet
40	3636	99.5	695	4	AAE10632	Aae10632	Human	wil
41	3636	99.5	695	4	AAE06862	Aae06862	Human	wil
42	3636	99.5	695	4	AAE02584	Aae02584	Human	amy
43	3636	99.5	695	4	AAU06606	Aau06606	Human	Amy
44	3636	99.5	695	5	ABB78593	Abb78593	Human	APP
45	3636	99.5	695	5	AAG68315	Aag68315	Human	amy

# ALIGNMENTS

## RESULT 1

AAW88430

ID AAW88430 standard; protein; 697 AA.

XX

AC AAW88430;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP695-VF-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP695-VF-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX  
PD 30-MAR-2000.  
XX  
PF 23-SEP-1999; 99WO-US020881.  
XX  
PR 24-SEP-1998; 98US-0101594P.  
XX  
PA (PHAA ) PHARMACIA & UPJOHN CO.  
XX  
PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;  
XX  
DR WPI; 2000-303209/26.  
DR N-PSDB; AAA15667.  
XX  
PT New enzyme designated human aspartase useful in research into Alzheimer's  
PT Disease is capable of cleaving amyloid protein precursor at the beta  
PT secretase site to produce amyloid beta peptide.  
XX  
PS Claim 133; Page 148-153; 183pp; English.  
XX  
CC This sequence represents a modified version of the human amyloid  
CC precursor protein (APP) amino acid sequence. The sequence is used in an  
CC example of the method of the invention, to show that modification of APP  
CC increases beta amyloid protein processing. The invention relates to a  
CC protease (e.g. Asp2) capable of cleaving the beta secretase site of  
CC amyloid precursor protein (APP). The protease contains a sequence  
CC encoding the amino acid sequence DTG and a sequence encoding DSG or DTG  
CC separated by 100-300 amino acids. When mutated the APP gene causes an  
CC autosomal dominant form of Alzheimer's disease. APP localises to the cell  
CC surface membrane and have a single C-terminal transmembrane domain.  
CC Proteolytic processing of APP produces the amyloid beta protein, which is  
CC possibly very important in Alzheimer's disease. The invention includes a  
CC nucleotide sequence encoding the protease, a vector containing the  
CC nucleotide sequence, and a cell line comprising the vector. Methods for  
CC screening for inhibitors of beta secretase activity are also given in the  
CC invention. The human aspartase protein and nucleotide sequences and the  
CC methods for identifying inhibitors of the protease, are useful in the  
CC treatment of and research in to Alzheimer's disease  
XX  
SQ Sequence 697 AA;

Query Match 100.0%; Score 3653; DB 3; Length 697;  
Best Local Similarity 100.0%; Pred. No. 9e-254;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180

Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL VFFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHG	660
Db	601	RHDSGYEVHHQKL VFFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHG	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

# RESULT 2

AAU07210

ID AAU07210 standard; protein; 697 AA.

XX

AC AAU07210;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP695-VF-KK.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP695-VF-KK.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 642

FT /note= "Wild type Val substituted by Phe"

XX



PN WO200149097-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000797.

XX

PR 09-MAY-2001; 2001WO-IB000797.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502548/55.

DR N-PSDB; AAS11710.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
PT activity.

XX

PS Example 8; Page 150-152; 185pp; English.

XX

CC The invention relates to a novel purified polypeptide comprising a  
CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the  
CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide  
CC and the fragment retain the beta-secretase activity of the mammalian Asp2  
CC protein. Also included is an isoform of amyloid protein precursor (APP)  
CC comprising the amino acid sequence of a APP or its fragment containing an  
CC APP cleavage site recognisable by a mammalian beta-secretase, and further  
CC comprising two lysine residues at the carboxyl terminus of the amino acid  
CC sequence of the mammalian APP or APP fragment. The polypeptides are used  
CC for assaying for modulators of beta-secretase activity; identifying  
CC agents that inhibit the APP processing activity of human Asp2 aspartyl  
CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2  
CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.  
CC Agents identified by the above methods are useful for treating  
CC Alzheimer's disease; and for identifying modulators of amyloid-beta  
CC (Abeta) peptide production, for use in designing therapeutics for the  
CC treatment or prevention of Alzheimer's disease. Probes and primers  
CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp  
CC nucleic acids in in vitro assays and in Northern and Southern blots. The  
CC present sequence represents the amino acid sequence of human amyloid  
CC protein precursor, APP695-VF-KK, used in the method of the invention

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3653; DB 4; Length 697;

Best Local Similarity 100.0%; Pred. No. 9e-254;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPVEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPVEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 3

AAE10637

ID AAE10637 standard; protein; 697 AA.

XX

AC AAE10637;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-VF-KK (APP695-VF-KK) isoform.

XX

KW Human; aspartyl protease 1; Aspl; amyloid precursor protein;

KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;  
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;  
KW APP695-VF-KK; mutant; mutein.  
XX  
OS Homo sapiens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Misc-difference 642  
FT /note= "Wild-type Val substituted with Phe"  
XX  
PN GB2357767-A.  
XX  
PD 04-JUL-2001.  
XX  
PF 22-SEP-2000; 2000GB-00023315.  
XX  
PR 23-SEP-1999; 99US-00404133.  
PR 23-SEP-1999; 99US-0155493P.  
PR 23-SEP-1999; 99WO-US020881.  
PR 13-OCT-1999; 99US-00416901.  
PR 06-DEC-1999; 99US-0169232P.  
XX  
PA (PHAA ) PHARMACIA & UPJOHN CO.  
XX  
PI Bienkowski MJ, Gurney M;  
XX  
DR WPI; 2001-444208/48.  
DR N-PSDB; AAD17873.  
XX  
PT Polypeptide comprising fragments of human aspartyl protease with amyloid  
PT precursor protein processing activity and alpha-secretase activity, for  
PT identifying modulators useful in treating Alzheimer's disease.  
XX  
PS Example 8; Page 120-122; 187pp; English.  
XX  
CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1  
CC proteins which lack transmembrane domain or amino terminal domain or  
CC cytoplasmic domain and retains alpha-secretase activity and amyloid  
CC protein precursor (APP) processing activity. The proteins of the  
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which  
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase  
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity  
CC are useful for treating Alzheimer's disease (AD) which causes progressive  
CC dementia with consequent formation of amyloid plaques, neurofibrillary  
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful  
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein  
CC with the substrate under acidic conditions and determining the level of  
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid  
CC protein precursor 695-VF-KK (APP695-VF-KK) isoform. This sequence is  
CC obtained by the addition of two lysine residues (KK motif) at the C-  
CC terminus of App695-VF isoform which is generated by the London mutation  
CC in APP695, where Val at position 642 is replaced with Phe. APP695-VF-KK  
CC isoform is useful for assaying the beta-secretase activity of human  
CC aspartyl protease 2a (hu-Asp2a) protein  
XX  
SQ Sequence 697 AA;

Query Match 100.0%; Score 3653; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 9e-254;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPG LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||||||
Db      1 MLPG LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      |||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480
      |||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL 540
      |||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMP SLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      |||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660
      |||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQNKK 697
      |||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQNKK 697
```

RESULT 4

AAE06867

ID AAE06867 standard; protein; 697 AA.

XX  
 AC AAE06867;  
 XX  
 DT 23-OCT-2001 (first entry)  
 XX  
 DE Human amyloid precursor protein 695-VF-KK (APP695-VF-KK) isoform.  
 XX  
 KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-VF-KK;  
 KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;  
 KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;  
 KW neuroprotective; antisense therapy; gene therapy; APP695-VF-KK; mutant;  
 KW mutein.  
 XX  
 OS Homo sapiens.  
 OS Synthetic.  
 XX  
 FH Key Location/Qualifiers  
 FT Misc-difference 642  
 FT /note= "Wild type Val substituted with Phe"  
 XX  
 PN WO200150829-A2.  
 XX  
 PD 19-JUL-2001.  
 XX  
 PF 09-MAY-2001; 2001WO-IB000799.  
 XX  
 PR 09-MAY-2001; 2001WO-IB000799.  
 XX  
 PA (BIEN/) BIENKOWSKI M J.  
 PA (GURN/) GURNEY M E.  
 PA (HEIN/) HEINRIKSON R L.  
 PA (PARO/) PARODI L A.  
 PA (YANR/) YAN R.  
 XX  
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;  
 XX  
 DR WPI; 2001-483072/52.  
 DR N-PSDB; AAD13029.  
 XX  
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
 PT activity.  
 XX  
 PS Example 8; Page 150-152; 185pp; English.  
 XX  
 CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid  
 CC precursor protein (APP) isoforms and their corresponding DNA molecules.  
 CC Human aspartyl proteases can act as beta-secretase proteases useful for  
 CC treating Alzheimer's disease. APP isoforms are useful for identifying  
 CC modulators of amyloid-beta peptide production, for use in designing  
 CC therapeutics for the treatment and prevention of Alzheimer's disease,  
 CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis  
 CC and neuronal loss. APP isoforms are also used in methods for identifying  
 CC inhibitors and modulators of human Asp2 activity. The invention relates  
 CC to a method for identifying agents that modulate the activity of human  
 CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used

CC as a means to screen in cellular assays for the inhibitors of beta- and  
CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in  
CC polymerase chain reactions (PCR). The probes are useful for detecting Hu-  
CC Asp nucleic acids in in vitro assays and in Northern and Southern blots.  
CC The present sequence is modified human amyloid precursor protein 695-VF-  
CC KK (APP695-VF-KK) isoform. APP695-VF-KK isoform is obtained by addition  
CC of two Lys residues (KK motif) at the C-terminal end of APP695-VF  
CC isoform. APP695-VF isoform is obtained by London V-F mutation in APP695  
CC isoform, where Val at position 642 is replaced with Phe. APP695-VF-KK  
CC isoform is useful for assaying the beta-secretase activity of human  
CC aspartyl protease 2a (Hu-Asp2a) protein  
XX  
SQ Sequence 697 AA;

Query Match 100.0%; Score 3653; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 9e-254;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660  
 |||||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697  
 |||||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 5

AAE02589

ID AAE02589 standard; protein; 697 AA.

XX

AC AAE02589;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-VF-KK (APP695-VF-KK).

XX

KW Human; alpha-secretase; therapy; amyloid precursor protein 695-VF-KK;

KW APP695-VF-KK; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.

XX

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney M, Bienkowski MJ;

XX

DR WPI; 2001-290516/30.

DR N-PSDB; AAD06747.

XX

PT Enzymes that cleave the alpha-secretase site of the amyloid precursor  
 PT protein, useful for the treatment of Alzheimer's disease.

XX

PS Example 8; Page 149-151; 189pp; English.

XX

CC The present invention relates to enzymes for cleaving the alpha-  
 CC secretase site of the amyloid precursor protein (APP) and methods of  
 CC identifying those enzymes. The methods may be used to identify enzymes  
 CC that may be used to cleave the alpha-secretase cleavage site of the APP  
 CC protein. The enzymes may be used to treat or modulate the progress of  
 CC Alzheimer's disease. The present sequence is human APP695-VF-KK. This  
 CC sequence is characterised by a V to F alteration at position 642 and  
 CC contains two carboxy-terminal lysine residues

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3653; DB 4; Length 697;

Best Local Similarity 100.0%; Pred. No. 9e-254;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

RESULT 6



AAU06611

ID AAU06611 standard; protein; 697 AA.

XX

AC AAU06611;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-VF-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;  
KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;  
KW amyloid-beta; Abeta; APP695-VF-KK; London mutant; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 642

FT /note= "Wild-type Val substituted by Phe"

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

DR N-PSDB; AAS11525.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl  
PT protease 2, lacking Asp2 transmembrane domain and retaining beta  
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2  
PT activity.

XX

PS Example 8; Page 150-152; 185pp; English.

XX

CC The invention relates to a purified polypeptide comprising a fragment of  
CC mammalian aspartyl protease (Asp2) protein which lacks the Asp2  
CC transmembrane domain and the Asp2 protein, and where the polypeptide and  
CC the fragment retain the beta-secretase activity of the mammalian Asp2  
CC protein. The invention also details polynucleotides for the Asp proteins  
CC and vectors expressing them, and a polypeptide (isoform of amyloid  
CC protein precursor (APP)) comprising the amino acid sequence of an APP or  
CC its fragment containing an APP cleavage site recognizable by a mammalian  
CC beta-secretase, and further comprising two lysine residues at the



Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 |||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660  
 |||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697

RESULT 7

ABB78598

ID ABB78598 standard; protein; 697 AA.

XX

AC ABB78598;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-VF-KK protein sequence SEQ ID NO:20.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;  
 KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52465.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
 PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 8; Page 120-122; 182pp; English.

XX



Db 361 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540  
 Qy 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660  
 Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697  
 ||||||||||||||||||||||||||||||||||||||||||||  
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 8

AAV88428

ID AAV88428 standard; protein; 697 AA.

XX

AC AAV88428;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP696-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP696-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX

PD 30-MAR-2000.

XX

PF 23-SEP-1999; 99WO-US020881.

XX

PR 24-SEP-1998; 98US-0101594P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2000-303209/26.

DR N-PSDB; AAA15665.

XX

PT New enzyme designated human aspartase useful in research into Alzheimer's

PT Disease is capable of cleaving amyloid protein precursor at the beta

PT secretase site to produce amyloid beta peptide.

XX



Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
 Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH HGV 660  
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660  
 Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 ||||||||||||||||||||||||||||||||||||||||||||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 9

AAU07208

ID AAU07208 standard; protein; 697 AA.

XX

AC AAU07208;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP695-KK.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP695-KK.

XX

OS Homo sapiens.

XX

PN WO200149097-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000797.

XX

PR 09-MAY-2001; 2001WO-IB000797.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502548/55.

DR N-PSDB; AAS11708.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2





Db	361	QEKVESLEQEAA <sup>     </sup> NERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Qy	481	EEIQDEVDELLQKEQNYSDDVLANMISEPRISYGN <sup>     </sup> DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDVLANMISEPRISYGN <sup>     </sup> DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV <sup>     </sup> PANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV <sup>     </sup> PANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL <sup>     </sup> VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH <sup>     </sup> HGV	660
Db	601	RHDSGYEVHHQKL <sup>     </sup> VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH <sup>     </sup> HGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 10

AAE10635

ID AAE10635 standard; protein; 697 AA.

XX

AC AAE10635;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease 1; Aspl; amyloid precursor protein; APP695-KK;

KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;

KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN GB2357767-A.

XX

PD 04-JUL-2001.

XX

PF 22-SEP-2000; 2000GB-00023315.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2001-444208/48.

DR N-PSDB; AAD17871.

XX

PT Polypeptide comprising fragments of human aspartyl protease with amyloid  
PT precursor protein processing activity and alpha-secretase activity, for  
PT identifying modulators useful in treating Alzheimer's disease.

XX

PS Example 6; Page 114-116; 187pp; English.

XX

CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1  
CC proteins which lack transmembrane domain or amino terminal domain or  
CC cytoplasmic domain and retains alpha-secretase activity and amyloid  
CC protein precursor (APP) processing activity. The proteins of the  
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which  
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase  
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity  
CC are useful for treating Alzheimer's disease (AD) which causes progressive  
CC dementia with consequent formation of amyloid plaques, neurofibrillary  
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful  
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein  
CC with the substrate under acidic conditions and determining the level of  
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid  
CC protein precursor 695-KK (APP695-KK) isoform which is obtained by the  
CC addition of two Lys residues (KK motif) at the C-terminus of APP695  
CC protein

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3646; DB 4; Length 697;

Best Local Similarity 99.9%; Pred. No. 2.9e-253;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
          ||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
```

Db	361	 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV	660
Db	601	 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 11

AAE06865

ID AAE06865 standard; protein; 697 AA.

XX

AC AAE06865;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-KK;  
 KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;  
 KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;  
 KW neuroprotective; antisense therapy; gene therapy; APP695-KK; mutant;  
 KW mutein.

XX

OS Homo sapiens.

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX  
DR WPI; 2001-483072/52.  
DR N-PSDB; AAD13027.

The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid precursor protein (APP) isoforms and their corresponding DNA molecules. Human aspartyl proteases can act as beta-secretase proteases useful for treating Alzheimer's disease. APP isoforms are useful for identifying modulators of amyloid-beta peptide production, for use in designing therapeutics for the treatment and prevention of Alzheimer's disease, dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis and neuronal loss. APP isoforms are also used in methods for identifying inhibitors and modulators of human Asp2 activity. The invention relates to a method for identifying agents that modulate the activity of human aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used as a means to screen in cellular assays for the inhibitors of beta- and gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in polymerase chain reactions (PCR). The probes are useful for detecting Hu-Asp nucleic acids in in vitro assays and in Northern and Southern blots. The present sequence is modified human amyloid precursor protein 695-KK (APP695-KK) isoform. APP695-KK isoform is obtained by addition of two Lys residues (KK motif) at the C-terminal end of APP695 isoform

XX  
SQ Sequence 697 AA;

Query Match 99.8%; Score 3646; DB 4; Length 697;  
Best Local Similarity 99.9%; Pred. No. 2.9e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWSDSPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWSDSPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDGDGEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDGEVEEEAEEPYYEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFOKAKERLEAKHRERMSOVMREWEEAEROAKNLPKADKKAVIOHF	360

Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 12

AAE02587

ID AAE02587 standard; protein; 697 AA.

XX

AC AAE02587;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-KK; APP695-KK; therapy; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.

XX

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Gurney M, Bienkowski MJ;  
 XX  
 DR WPI; 2001-290516/30.  
 DR N-PSDB; AAD06745.  
 XX  
 PT Enzymes that cleave the alpha-secretase site of the amyloid precursor  
 PT protein, useful for the treatment of Alzheimer's disease.  
 XX  
 PS Example 6; Page 143-145; 189pp; English.  
 XX  
 CC The present invention relates to enzymes for cleaving the alpha-  
 CC secretase site of the amyloid precursor protein (APP) and methods of  
 CC identifying those enzymes. The methods may be used to identify enzymes  
 CC that may be used to cleave the alpha-secretase cleavage site of the APP  
 CC protein. The enzymes may be used to treat or modulate the progress of  
 CC Alzheimer's disease. The present sequence is human APP695-KK. This  
 CC sequence contains two carboxy-terminal lysine residues  
 XX  
 SQ Sequence 697 AA;

Query Match 99.8%; Score 3646; DB 4; Length 697;  
 Best Local Similarity 99.9%; Pred. No. 2.9e-253;  
 Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL	540

```

      ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
Qy      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
      ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

```

RESULT 13

AAU06609

ID AAU06609 standard; protein; 697 AA.

XX

AC AAU06609;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

DR N-PSDB; AAS11523.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl





Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 14

ABB78596

ID ABB78596 standard; protein; 697 AA.

XX

AC ABB78596;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-KK protein sequence SEQ ID NO:16.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;  
KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.  
PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA ) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52463.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl  
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 6; Page 114-116; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)  
CC substrate (I) which comprises a peptide of no more than 50 amino acids,  
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-  
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1  
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with  
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1  
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a  
CC nucleotide sequence that hybridises under stringent conditions to the non  
CC -coding strand complementary to a defined 1804 nucleotide sequence (see  
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1  
CC proteolytic activity and lacks nucleotides encoding a transmembrane  
CC domain); (3) a purified polynucleotide (III') comprising a sequence that  
CC hybridises under stringent conditions to (III) (the nucleotide sequence  
CC encodes a polypeptide further lacking a pro-peptide domain corresponding  
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)  
CC comprising (III) or (III'); and (5) a host cell (V) transformed or  
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease  
CC substrate (I) may be used as an enzyme substrate in assays to detect  
CC aspartyl protease activity, (II) and therefore diagnose diseases  
CC associated with aberrant hu-Asp1 expression and activity such as  
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while  
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present  
CC sequence represents human amyloid precursor protein APP695-KK, which is  
CC given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3646; DB 5; Length 697;  
Best Local Similarity 99.9%; Pred. No. 2.9e-253;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPGSK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPGSK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180

Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

# RESULT 15

AAW19484

ID AAW19484 standard; protein; 695 AA.

XX

AC AAW19484;

XX

DT 08-SEP-1997 (first entry)

XX

DE APP695 mutant A-beta-containing protein.

XX

KW Alzheimer's disease; transgenic mammal; beta-amyloid precursor protein;

KW APP.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 642

FT /note= "Wild-type Val is preferably substituted by Phe"

XX



Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

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 Job time : 50.3333 secs

GenCore version 5.1.6  
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OM protein - protein search, using sw model

Run on: July 26, 2004, 12:41:23 ; Search time 15 Seconds  
(without alignments)  
2398.887 Million cell updates/sec

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Perfect score: 3653  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Issued\_Patents\_AA:\*  
1: /cgn2\_6/ptodata/2/iaa/5A\_COMB.pep:\*  
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3: /cgn2\_6/ptodata/2/iaa/6A\_COMB.pep:\*  
4: /cgn2\_6/ptodata/2/iaa/6B\_COMB.pep:\*  
5: /cgn2\_6/ptodata/2/iaa/PCTUS\_COMB.pep:\*  
6: /cgn2\_6/ptodata/2/iaa/backfiles1.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	3653	100.0	697	4	US-09-548-372D-20	Sequence 20, Appl
2	3653	100.0	697	4	US-09-548-367D-20	Sequence 20, Appl
3	3653	100.0	697	4	US-09-551-853D-20	Sequence 20, Appl
4	3646	99.8	697	4	US-09-548-372D-16	Sequence 16, Appl
5	3646	99.8	697	4	US-09-548-367D-16	Sequence 16, Appl
6	3646	99.8	697	4	US-09-551-853D-16	Sequence 16, Appl
7	3643	99.7	695	4	US-09-548-372D-14	Sequence 14, Appl
8	3643	99.7	695	4	US-09-548-367D-14	Sequence 14, Appl
9	3643	99.7	695	4	US-09-551-853D-14	Sequence 14, Appl
10	3638	99.6	697	4	US-09-548-372D-18	Sequence 18, Appl
11	3638	99.6	697	4	US-09-548-367D-18	Sequence 18, Appl

12	3638	99.6	697	4	US-09-551-853D-18	Sequence 18, Appl
13	3636	99.5	695	1	US-08-123-702-2	Sequence 2, Appli
14	3636	99.5	695	2	US-08-104-165-1	Sequence 1, Appli
15	3636	99.5	695	3	US-08-464-250-1	Sequence 1, Appli
16	3636	99.5	695	4	US-08-464-250-1	Sequence 1, Appli
17	3636	99.5	695	4	US-09-458-481B-7	Sequence 7, Appli
18	3636	99.5	695	4	US-09-458-481B-8	Sequence 8, Appli
19	3636	99.5	695	4	US-09-548-372D-10	Sequence 10, Appl
20	3636	99.5	695	4	US-09-548-367D-10	Sequence 10, Appl
21	3636	99.5	695	4	US-09-551-853D-10	Sequence 10, Appl
22	3636	99.5	695	4	US-09-415-099-6	Sequence 6, Appli
23	3636	99.5	695	6	5218100-2	Patent No. 5218100
24	3630	99.4	694	1	US-08-339-152A-18	Sequence 18, Appl
25	3630	99.4	694	2	US-08-007-999B-5	Sequence 5, Appli
26	3630	99.4	694	2	US-08-689-276A-5	Sequence 5, Appli
27	3628	99.3	695	4	US-09-548-372D-12	Sequence 12, Appl
28	3628	99.3	695	4	US-09-548-367D-12	Sequence 12, Appl
29	3628	99.3	695	4	US-09-551-853D-12	Sequence 12, Appl
30	3624	99.2	695	1	US-08-371-930-27	Sequence 27, Appl
31	3624	99.2	695	5	PCT-US94-01712-27	Sequence 27, Appl
32	3612	98.9	695	1	US-08-339-152A-30	Sequence 30, Appl
33	3607	98.7	753	4	US-09-548-372D-61	Sequence 61, Appl
34	3607	98.7	753	4	US-09-548-367D-61	Sequence 61, Appl
35	3607	98.7	753	4	US-09-551-853D-61	Sequence 61, Appl
36	3597	98.5	751	1	US-08-123-702-4	Sequence 4, Appli
37	3597	98.5	751	2	US-08-104-165-2	Sequence 2, Appli
38	3597	98.5	751	2	US-08-422-333-2	Sequence 2, Appli
39	3597	98.5	751	2	US-08-422-333-21	Sequence 21, Appl
40	3597	98.5	751	3	US-08-464-250-2	Sequence 2, Appli
41	3597	98.5	751	4	US-08-464-250-2	Sequence 2, Appli
42	3597	98.5	751	4	US-08-832-867-5	Sequence 5, Appli
43	3597	98.5	751	4	US-09-548-372D-57	Sequence 57, Appl
44	3597	98.5	751	4	US-09-548-367D-57	Sequence 57, Appl
45	3597	98.5	751	4	US-09-551-853D-57	Sequence 57, Appl

#### ALIGNMENTS

##### RESULT 1

US-09-548-372D-20

; Sequence 20, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR  
AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-372D-20

Query Match 100.0%; Score 3653; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 8.1e-268;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660



Db 241 EADDDDEDDGDEVEEEAEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

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 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
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 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
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 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
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 Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540  
 Qy 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
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 Db 541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHGGV 660  
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 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHGGV 660  
 Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697  
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 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 3

US-09-551-853D-20

; Sequence 20, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-20

Query Match 100.0%; Score 3653; DB 4; Length 697;  
Best Local Similarity 100.0%; Pred. No. 8.1e-268;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

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Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660

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Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
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RESULT 4  
US-09-548-372D-16  
; Sequence 16, Application US/09548372D

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; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-372D-16

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Query Match          99.8%; Score 3646; DB 4; Length 697;
Best Local Similarity 99.9%; Pred. No. 2.8e-267;
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
|
Db    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
|
Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
|
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
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Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
|
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

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Qy      421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db      421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660
        |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697
        |||
Db      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

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RESULT 5

US-09-548-367D-16

; Sequence 16, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-367D-16

Query Match 99.8%; Score 3646; DB 4; Length 697;

Best Local Similarity 99.9%; Pred. No. 2.8e-267;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

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Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 6

US-09-551-853D-16

; Sequence 16, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: US 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: US 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-551-853D-16

Query Match 99.8%; Score 3646; DB 4; Length 697;  
Best Local Similarity 99.9%; Pred. No. 2.8e-267;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600

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          |||
Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVKMDAEF 600
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660
          |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
          |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 7

US-09-548-372D-14

; Sequence 14, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 14

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-14

Query Match 99.7%; Score 3643; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 4.6e-267;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDS DPSG TK 60
          |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDS DPSG TK 60
Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||
Db      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
          |||
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

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Db	181		240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241		300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301		360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421		480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481		540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541		600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV	660
Db	601		660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661		695

RESULT 8

US-09-548-367D-14

; Sequence 14, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 14  
; LENGTH: 695  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-367D-14

Query Match 99.7%; Score 3643; DB 4; Length 695;  
Best Local Similarity 100.0%; Pred. No. 4.6e-267;  
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
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## RESULT 9

US-09-551-853D-14

; Sequence 14, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 14

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-14

Query Match 99.7%; Score 3643; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 4.6e-267;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||

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Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||

Db 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTELLPVNGEFSL 540  
 |||

Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||

Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660  
 |||

Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQN 695  
 |||

Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQN 695

RESULT 10

US-09-548-372D-18

; Sequence 18, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-18

Query Match 99.6%; Score 3638; DB 4; Length 697;  
 Best Local Similarity 99.6%; Pred. No. 1.1e-266;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 11

US-09-548-367D-18

; Sequence 18, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

```

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-367D-18

```

```

Query Match          99.6%; Score 3638; DB 4; Length 697;
Best Local Similarity 99.6%; Pred. No. 1.1e-266;
Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA 480

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Qy      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
          |||
Db      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
          |||
Db      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy      601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV 660
          |||
Db      601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFE QMQNKK 697
          |||
Db      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFE QMQNKK 697

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RESULT 12

US-09-551-853D-18

; Sequence 18, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-18

Query Match 99.6%; Score 3638; DB 4; Length 697;

Best Local Similarity 99.6%; Pred. No. 1.1e-266;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
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Db      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

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Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
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Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLOKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLOKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
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Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 13

US-08-123-702-2

; Sequence 2, Application US/08123702

; Patent No. 5604131

; GENERAL INFORMATION:

; APPLICANT: Wadsworth, Samuel

; APPLICANT: Snyder, Benjamin

; APPLICANT: Reddy, Vermuri, B.

; APPLICANT: Wei, Chamer

; TITLE OF INVENTION: A cDNA Genomic Hybrid Sequence Encoding APP770

; Patent No. 5604131

; TITLE OF INVENTION: Containing a Genomic DNA Insert of the KI and OX-2 Regions

; NUMBER OF SEQUENCES: 45

; CORRESPONDENCE ADDRESS:







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; APPLICATION NUMBER: 9118445.7
; FILING DATE: 28-AUG-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Liebeschuetz, Joe
; REGISTRATION NUMBER: 37,505
; REFERENCE/DOCKET NUMBER: 16163-000100
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (415) 326-2400
; TELEFAX: (415) 326-2422
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 695 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-104-165-1

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Query Match          99.5%; Score 3636; DB 2; Length 695;
Best Local Similarity 99.9%; Pred. No. 1.6e-266;
Matches 694; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Db      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
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Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE 240
        |||
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Qy      241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db      241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

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        |||
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 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695

RESULT 15

US-08-464-250-1

; Sequence 1, Application US/08464250  
 ; Patent No. 6107542  
 ; GENERAL INFORMATION:  
 ; APPLICANT: HARDY, John Anthony  
 ; APPLICANT: GOATE, Alison Mary  
 ; APPLICANT: MULLAN, Michael John  
 ; APPLICANT: CHARTIER-HARLIN, Marie-Christine  
 ; APPLICANT: OWEN, Michael John  
 ; TITLE OF INVENTION: Test and Model for Alzheimer's Disease  
 ; NUMBER OF SEQUENCES: 44  
 ; CORRESPONDENCE ADDRESS:  
 ; ADDRESSEE: Townsend and Townsend Khourie and Crew  
 ; STREET: 379 Lytton Avenue  
 ; CITY: Palo Alto  
 ; STATE: California  
 ; COUNTRY: US  
 ; ZIP: 94301  
 ; COMPUTER READABLE FORM:  
 ; MEDIUM TYPE: Floppy Disk  
 ; COMPUTER: IBM PC compatible  
 ; OPERATING SYSTEM: PC-DOS/MS-DOS  
 ; CURRENT APPLICATION DATA:  
 ; APPLICATION NUMBER: US/08/464,250  
 ; FILING DATE: 05-JUN-1995  
 ; CLASSIFICATION: 435  
 ; PRIOR APPLICATION DATA:  
 ; APPLICATION NUMBER: 08/104,165  
 ; FILING DATE: 21-JAN-1992  
 ; APPLICATION NUMBER: 9101307.8  
 ; FILING DATE: 21-JAN-1991  
 ; APPLICATION NUMBER: 9118445.7  
 ; FILING DATE: 28-AUG-1991  
 ; ATTORNEY/AGENT INFORMATION:  
 ; NAME: Liebeschuetz, Joe  
 ; REGISTRATION NUMBER: 37,505  
 ; REFERENCE/DOCKET NUMBER: 16163-000100  
 ; TELECOMMUNICATION INFORMATION:  
 ; TELEPHONE: (415) 326-2400  
 ; TELEFAX: (415) 326-2422  
 ; INFORMATION FOR SEQ ID NO: 1:  
 ; SEQUENCE CHARACTERISTICS:

; LENGTH: 695 amino acids  
; TYPE: amino acid  
; STRANDEDNESS: single  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
US-08-464-250-1

Query Match 99.5%; Score 3636; DB 3; Length 695;  
Best Local Similarity 99.9%; Pred. No. 1.6e-266;  
Matches 694; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
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Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
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        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

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Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
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Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

Search completed: July 26, 2004, 12:48:23  
Job time : 17 secs

GenCore version 5.1.6  
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:40:23 ; Search time 13.6667 Seconds  
(without alignments)  
4905.768 Million cell updates/sec

Title: US-09-806-194A-20  
Perfect score: 3653  
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Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : PIR 78:\*  
1: pir1:\*  
2: pir2:\*  
3: pir3:\*  
4: pir4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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		Match	Length			
1	3636	99.5	695	1	A49795	Alzheimer's diseas
2	3585.5	98.2	770	1	QRHUA4	Alzheimer's diseas
3	3539	96.9	695	2	S00550	Alzheimer's diseas
4	3514	96.2	695	2	A27485	Alzheimer's diseas
5	3098	84.8	747	2	JH0773	Alzheimer's diseas
6	2105	57.6	484	4	A32761	hypothetical Alzhe
7	1723	47.2	763	2	A49321	amyloid beta (A4)
8	1711	46.8	765	2	S42880	amyloid precursor-
9	1699	46.5	751	2	A49974	beta-amyloid precu
10	1180	32.3	653	2	A46362	amyloid precursor-
11	1138	31.2	511	2	JC1404	CDEI-box DNA-bindi
12	816.5	22.4	686	2	T15795	hypothetical prote
13	754	20.6	886	2	A32758	beta-amyloid-like

14	706	19.3	246	2	S38344	CDEI-binding prote
15	406	11.1	82	2	PQ0438	Alzheimer's diseas
16	291.5	8.0	191	2	A35981	sperm membrane pro
17	278	7.6	57	2	E60045	Alzheimer's diseas
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20	278	7.6	57	2	D60045	Alzheimer's diseas
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23	217	5.9	42	2	PN0512	beta-amyloid prote
24	192.5	5.3	1110	2	I51116	NF-180 - sea lampr
25	185.5	5.1	407	1	EDBEQ3	immediate-early pr
26	184	5.0	5170	2	T15348	hypothetical prote
27	182	5.0	522	2	T32444	hypothetical prote
28	180.5	4.9	993	2	S49461	synaptonemal compl
29	179.5	4.9	1188	2	T46608	zinc finger protei
30	175.5	4.8	802	1	S48529	NAB3 protein - yea
31	174.5	4.8	464	2	H90279	microtubule bindin
32	174.5	4.8	884	2	T20405	hypothetical prote
33	174	4.8	579	2	JH0820	160K golgi antigen
34	174	4.8	1087	2	T30330	gelsolin-related p
35	174	4.8	1271	2	A45555	glutamate rich pro
36	173.5	4.7	793	1	JH0628	caldesmon - human
37	173	4.7	1187	2	T46637	transcription fact
38	172	4.7	771	1	A33430	h-caldesmon - chic
39	172	4.7	784	2	PN0009	neurofilament trip
40	172	4.7	1182	2	T30189	myelin transcripti
41	169.5	4.6	298	1	TPHUTC	troponin T, cardia
42	169.5	4.6	721	2	S29795	hypothetical prote
43	169	4.6	885	2	G71608	ATP-dept. acyl-CoA
44	168.5	4.6	675	2	T03744	myoD protein inhib
45	168.5	4.6	913	2	T52485	neurofilament prot

# ALIGNMENTS

## RESULT 1

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence\_revision 10-Sep-1999 #text\_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991

A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.

A;Reference number: A49795; MUID:91273117; PMID:1905108

A;Accession: A49795

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-695 <POD>

A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing



Query Match 99.5%; Score 3636; DB 1; Length 695;  
 Best Local Similarity 99.9%; Pred. No. 4e-184;  
 Matches 694; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
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Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLVFVFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

## RESULT 2

QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human

N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)

N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)

C;Species: Homo sapiens (man)

C;Date: 30-Jun-1987 #sequence\_revision 28-Jul-1995 #text\_change 15-Sep-2000

C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644

R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.

Nucleic Acids Res. 17, 517-522, 1989

A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.

A;Reference number: S02260; MUID:89128427; PMID:2783775

A;Accession: S02260

A;Molecule type: DNA

A;Residues: 1-288, 'V', 365-770 <LEM1>

A;Cross-references: EMBL:X13466

A;Note: alternative splice form APP(695)

R;Lemaire, H.G.

submitted to the EMBL Data Library, November 1988

A;Reference number: S05194

A;Accession: S05194

A;Molecule type: DNA

A;Residues: 1-14, 'VW', 17-288, 'V', 365-770 <LEM2>

A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360

A;Note: alternative splice form APP(695)

R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.

Biochem. Biophys. Res. Commun. 159, 297-304, 1989

A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.

A;Reference number: A32277; MUID:89165870; PMID:2538123

A;Accession: A32277

A;Molecule type: DNA

A;Residues: 1-75 <LAF>

A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074

R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.

Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989

A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.

A;Reference number: A33260; MUID:89392030; PMID:2675837

A;Accession: A33260

A;Molecule type: DNA

A;Residues: 656-737 <JOH>

A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865

R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.

Biochem. Biophys. Res. Commun. 170, 301-307, 1990

A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.

A;Reference number: A35486; MUID:90321244; PMID:2196878  
 A;Accession: A35486  
 A;Molecule type: DNA  
 A;Residues: 672-710 <PRE1>  
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 87, 257-263, 1990  
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.  
 A;Reference number: I39451; MUID:90236318; PMID:2110105  
 A;Accession: I39452  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-770 <YOS1>  
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616  
 A;Accession: I39451  
 A;Status: nucleic acid sequence not shown; translation not shown; translated  
 from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 1-530,'QWLMPVIPAFWEAKVGR' <YOS2>  
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615  
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.  
 Gene 102, 291-292, 1991  
 A;Reference number: A59020; MUID:91340168; PMID:1908403  
 A;Contents: annotation; erratum  
 A;Note: revised physical map for reference I39451  
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;  
 van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.  
 Science 248, 1124-1126, 1990  
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral  
 hemorrhage, Dutch type.  
 A;Reference number: I39453; MUID:90260663; PMID:2111584  
 A;Accession: I39453  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 656-737 <LEV>  
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620  
 A;Note: a mutation with 693-Gln is presented  
 R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.  
 Science 254, 97-99, 1991  
 A;Title: A mutation in the amyloid precursor protein associated with hereditary  
 Alzheimer's disease.  
 A;Reference number: I59562; MUID:92022553; PMID:1925564  
 A;Accession: I59562  
 A;Status: translated from GB/EMBL/DDBJ  
 A;Molecule type: DNA  
 A;Residues: 689-716,'F',718-737 <MUR>  
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721  
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.;  
 Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.;  
 Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma,  
 V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.;  
 Schellenberg, G.D.  
 Am. J. Hum. Genet. 51, 998-1014, 1992  
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds  
 for the APP gene region.  
 A;Reference number: A44017; MUID:93035397; PMID:1415269

A;Accession: A44017  
 A;Molecule type: DNA  
 A;Residues: 687-692, 'G', 694-718 <KAM1>  
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378  
 A;Experimental source: familial Alzheimer disease family SB  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)  
 A;Accession: B44017  
 A;Molecule type: DNA  
 A;Residues: 687-718 <KAM2>  
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380  
 A;Experimental source: familial Alzheimer disease family LIT  
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)  
 A;Note: this sequence has a silent mutation  
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.; Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B. Nature 325, 733-736, 1987  
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor.  
 A;Reference number: A03134; MUID:87144572; PMID:2881207  
 A;Accession: A03134  
 A;Molecule type: mRNA  
 A;Residues: 1-288, 'V', 365-770 <KAN>  
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526  
 A;Note: alternative splice form APP(695)  
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M. Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987  
 A;Title: Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides.  
 A;Reference number: A29030; MUID:87231971; PMID:3035574  
 A;Accession: A29030  
 A;Molecule type: mRNA  
 A;Residues: 284-288, 'V', 365-646, 'E', 648-770 <ROB>  
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540  
 A;Note: the authors translated the codon GAG for residue 647 as Asp  
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C. Science 235, 877-880, 1987  
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease.  
 A;Reference number: A47584; MUID:87120328; PMID:3810169  
 A;Accession: A47584  
 A;Molecule type: mRNA  
 A;Residues: 674-756, 'S', 758-770 <GOL>  
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707  
 A;Experimental source: brain  
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop, P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L. Science 235, 880-884, 1987  
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage near the Alzheimer locus.  
 A;Reference number: A47585; MUID:87120329; PMID:2949367  
 A;Accession: A47585  
 A;Molecule type: mRNA  
 A;Residues: 674-703 <TAN1>  
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958  
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang, J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K. EMBO J. 7, 949-957, 1988

A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.  
 A;Reference number: S02638; MUID:88296437; PMID:2900137  
 A;Accession: S02638  
 A;Molecule type: mRNA  
 A;Residues: 672-678 <DYZ>  
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.  
 Nature 331, 528-530, 1988  
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.  
 A;Reference number: S00707; MUID:88122640; PMID:2893290  
 A;Accession: S00707  
 A;Molecule type: mRNA  
 A;Residues: 286-344,'I',365-366 <TAN2>  
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612  
 A;Experimental source: promyelocytic leukemia cell line HL60  
 A;Note: alternative splice form APP(751)  
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.  
 Nature 331, 525-527, 1988  
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.  
 A;Reference number: S00925; MUID:88122639; PMID:2893289  
 A;Accession: S00925  
 A;Molecule type: mRNA  
 A;Residues: 1-344,'I',365-770 <PO2>  
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721  
 A;Note: alternative splice form APP(751)  
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.  
 Nature 331, 530-532, 1988  
 A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.  
 A;Reference number: A38949; MUID:88122641; PMID:2893291  
 A;Accession: A38949  
 A;Molecule type: mRNA  
 A;Residues: 287-367 <KIT>  
 A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611  
 A;Experimental source: glioblastoma cell line  
 A;Note: alternative splice form APP(770)  
 R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.  
 Brain Res. Mol. Brain Res. 4, 121-131, 1988  
 A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.  
 A;Reference number: A30320  
 A;Accession: A30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 284-288,'V',365-770 <VIT1>  
 A;Accession: B30320  
 A;Status: not compared with conceptual translation  
 A;Molecule type: mRNA  
 A;Residues: 122-288,'V',365-770 <VIT2>  
 A;Accession: C30320  
 A;Status: not compared with conceptual translation

A;Molecule type: mRNA  
A;Residues: 606-770 <VIT3>  
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.  
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988  
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.  
A;Reference number: A31087; MUID:88124954; PMID:2893379  
A;Accession: A31087  
A;Molecule type: mRNA  
A;Residues: 507-770 <ZAI>  
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573  
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser  
A;Note: the cited Genbank accession number, J03594, is not in release 101.0  
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

Query Match 98.2%; Score 3585.5; DB 1; Length 770;  
Best Local Similarity 90.0%; Pred. No. 2.1e-181;  
Matches 693; Conservative 1; Mismatches 1; Indels 75; Gaps 1;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
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Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
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Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLLKTTQEPLARD 360

Qy    289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345
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Db    361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy    346 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRRLALENYITAL 405
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Db    421 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRRLALENYITAL 480

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Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
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 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540

Qy 466 MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 525  
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 Db 541 MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 600

Qy 526 KTTVELLPVNGEFLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
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 Db 601 KTTVELLPVNGEFLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 660

Qy 586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645  
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 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720

Qy 646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
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 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

# RESULT 3

S00550

Alzheimer's disease amyloid beta protein precursor - rat

N;Alternate names: beta-A4 amyloid protein

C;Species: Rattus norvegicus (Norway rat)

C;Date: 30-Jun-1989 #sequence\_revision 30-Jun-1989 #text\_change 13-Aug-1999

C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.; Seeburg, P.H.

EMBO J. 7, 1365-1370, 1988

A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.

A;Reference number: S00550; MUID:88312583; PMID:2900758

A;Accession: S00550

A;Molecule type: mRNA

A;Residues: 1-695 <SHI>

A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617

R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.

Science 241, 223-226, 1988

A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.

A;Reference number: A41245; MUID:88264430; PMID:2968652

A;Accession: A41245

A;Molecule type: protein

A;Residues: 18-37, 'X', 39-40, 'X', 42-44 <SCH>

A;Note: evidence for heparan sulfate attachment

R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.

FEBS Lett. 349, 109-116, 1994

A;Title: The beta-A4 amyloid precursor protein binding to copper.

A;Reference number: S46251; MUID:94320627; PMID:7913895

A;Contents: annotation; copper binding sites

A;Note: rat peptides were isolated but not sequenced

R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.

J. Biol. Chem. 266, 8464-8469, 1991

A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.

F;625-648/Domain: transmembrane #status predicted <TMM>

Matches 675; Conservative 7; Mismatches 13; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
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Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDSIDSADAEEDSDVWVGADTDYADGGEDKVVEVAEEEEVADVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EAEDDEDVEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQOPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600



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Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGV 660
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Db      601 GHDSGFVVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
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Db      661 VEVDAAVTPEERHLSKMOONGYENPTYKFFEOMON 695

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#### RESULT 4

A27485

Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse

N;Alternate names: proteinase nexin II

C;Species: Mus musculus (house mouse)

C;Date: 31-Mar-1989 #sequence revision 31-Mar-1989 #text change 13-Aug-1999

C;Accession: A27485; S19727; I49485

R; Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.

Biochem. Biophys. Res. Commun. 149, 665-671, 1987

A;Title: Complementary DNA for the mouse homolog of the human amyloid beta protein precursor.

A;Reference number: A27485; MUID:88106489; PMID:3322280

A;Accession: A27485

A;Molecule type: mRNA

A;Residues: 1-695 <YAM>

A;Cross-references: GB:M18373; NID:q191568; PIDN:AAA37139.1; PID:q309085

A;Experimental source: brain

Ride Strooper, B.; van Leuven, F.; van den Berghe, H.

Biochim. Biophys. Acta 1129, 141-143, 1991

A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is closer related to its human homolog than previously reported.

A;Reference number: S19727; MUID:92096458; PMID:1756177

A;Accession: S19727

A;Molecule type: mRNA

A;Residues: 1-210, 'G', 212-220, 'S', 222-396, 'A', 398-402, 'T', 404-448, 'A', 450-695  
<STR>

A;Cross-references: EMBL:X59379

R; Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.  
Gene 112, 189-195, 1992

A;Title: Positive and negative regulatory elements for the expression of the Alzheimer's disease amyloid precursor-encoding gene in mouse.

A;Reference number: I49485; MUID:92209998; PMID:1555768

A;Accession: I49485

A;Status: translated from GB/EMBL/DDBJ

A:Molecule type: DNA

A:Residues: 1-19 &lt;RES&gt;

A;Cross-references: GB:D10603; NID:q220328; PIDN:BAA01456.1; PID:q220329

C;Genetics:

A;Map position: 16C3

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; amyloid; transmembrane protein

Query Match 96.2%; Score 3514; DB 2; Length 695;

Best Local Similarity 96.7%; Pred. No. 1.1e-177;

Matches 672; Conservative 5; Mismatches 18; Indels 0; Gaps 0;

Qy 1 MLPG LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDS DPSG TK 60

Db	1	MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGK	60
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Db	61	TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLP CGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDSVDSADAEEDSDVWVGADTDYADGGEDKVVEVAEEEEVADVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDVEDGDEVEEEAEPEYEEATERTTSTATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLDLENYIIALQAVPPRPHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKATQIRSQVMTHLRVIYERMNQSLSLLYNPVA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHG	660
Db	601	GHDSGFVVRHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

A;Title: A Xenopus homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.  
A;Reference number: JH0773; MUID:93129227; PMID:1282805  
A;Accession: JH0773  
A;Molecule type: mRNA  
A;Residues: 1-747 <OKA>  
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151  
A;Experimental source: larva  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
C;Keywords: alternative splicing; amyloid  
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 84.8%; Score 3098; DB 2; Length 747;  
Best Local Similarity 80.9%; Pred. No. 9.2e-156;  
Matches 597; Conservative 35; Mismatches 42; Indels 64; Gaps 5;

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Qy      17 ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCTCIDTKEGILQYCQE 75
      |||| ||| ||||||||| |||||||||::| || || |||||||||
Db      15 ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE 71

Qy      76 VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF 135
      |||||||||:|||||: | |:|||||||||||||||
Db      72 VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF 131

Qy     136 LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN 195
      |||||:|||||:|||| |:|:||||||||||||||| |||::
Db     132 LHQERMDICETHLHWHTVAKESCSSEKSM LHEYGMLLPCGIDKFRGVEFVCCPSAEES 191

Qy     196 VDSADAEEDSDVWVGADTDYADGSEDKVVEVA--EEEEVAEVEEEEADDDDEDDEDGDE 253
      ||||| ||| ||||||| || | |:| || || |||| | |||| | |||
Db     192 FDSADAAEDDCDVWVGADADYVDRSDDKAVEAQPDEEEEVVEVEEETDDDED--DGDE 249

Qy     254 VEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVR----- 288
      ||| |||||||||||||||||||||||||
Db     250 AEEPEEPYEEATERTTSIATTTTTTTTESVEEVVREVCSEQAETGPCRAMISRWYYDVTE 309

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQ 317
      :| ||||||||| | |||| |
Db     310 SKCAQFIYGGCGGNRNNFESDDYCMVCGSVIPATAASTPDAVDKYLENPNDENEHDFL 369

Qy     318 KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQ 377
      ||||| |||:|:|:|:|||||||||||||||||||||:|
Db     370 KAKERLEGKHKREKMSVMEKEWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAKQRQQ 429

Qy     378 LVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKH 437
      |||||||||:||||||| |||||||||||||||||
Db     430 LVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKH 489

Qy     438 EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNY 497
      ||||||||| ||||| |||| | ||||||||| |||||
Db     490 EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPVAVAEEIQDEVDELQKEQNY 549

Qy     498 SDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSV 557
      |||::|:|:| |:| |||||||||:|||||||:|:|:| |||||
Db     550 SDDMVSNMVS DHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLQPWHSFGVDSVPAN 609

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Qy      558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFA 617
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA 669

Qy      618 EDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKM 677
          |:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGVEVDAAVTPEERHLTKM 729

Qy      678 QQNGYENPTYKFFEQMQN 695
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      730 QQNGYENPTYKFFEQMQN 747

```

# RESULT 6

A32761

hypothetical Alzheimer's disease amyloid beta protein, Alu-containing clone - human (fragment)

C;Species: Homo sapiens (man)

C;Date: 29-Jan-1990 #sequence\_revision 10-Apr-1996 #text\_change 10-Apr-1996

C;Accession: A32761

R;de Sauvage, F.; Octave, J.N.

Science 245, 651-653, 1989

A;Title: A novel mRNA of the A4 amyloid precursor gene coding for a possibly secreted protein.

A;Reference number: A32761; MUID:89346754; PMID:2569763

A;Accession: A32761

A;Molecule type: mRNA

A;Residues: 1-484 <DES>

A;Cross-references: GB:M28373

A;Note: the authors translated the codon ATG for residue 433 as Leu

C;Comment: This is the hypothetical translation of a sequence believed to contain cloning artifacts.

C;Keywords: cloning artifact

Query Match 57.6%; Score 2105; DB 4; Length 484;

Best Local Similarity 87.7%; Pred. No. 1e-103;

Matches 407; Conservative 1; Mismatches 0; Indels 56; Gaps 1;

```

Qy      80 LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 139
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      1  LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 60

Qy      140 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 199
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      61 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 120

Qy      200 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDDGDEVEEEAE 259
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      121 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDDGDEVEEEAE 180

Qy      260 EPYEEATERTTSIATTTTTTTESVEEVVR----- 288
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      181 EPYEEATERTTSIATTTTTTTESVEEVVREVCSEAETGPCRAMISRWFVDTGKCAPF 240

Qy      289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 323
          :|||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      241 FYGGCGGNRNNFDTEEYCMVCGSAIPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 300

```

Qy 324 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 383  
 |||  
 Db 301 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 360

Qy 384 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 443  
 |||  
 Db 361 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 420

Qy 444 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 487  
 |||  
 Db 421 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 464

# RESULT 7

A49321

amyloid beta (A4) homolog 2 precursor - human

N;Alternate names: CDEI-binding protein

C;Species: Homo sapiens (man)

C;Date: 24-Feb-1994 #sequence\_revision 18-Nov-1994 #text\_change 13-Aug-1999

C;Accession: A49321; S34644; S40519

R;Sprecher, C.A.; Grant, F.J.; Grimm, G.; O'Hara, P.J.; Norris, F.; Norris, K.; Foster, D.C.

Biochemistry 32, 4481-4486, 1993

A;Title: Molecular cloning of the cDNA for a human amyloid precursor protein homolog: evidence for a multigene family.

A;Reference number: A49321; MUID:93250009; PMID:8485127

A;Accession: A49321

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <SPR>

A;Cross-references: GB:S60099; NID:g300168; PIDN:AAC60589.1; PID:g300169

A;Experimental source: placenta

A;Note: sequence extracted from NCBI backbone (NCBIN:131198, NCBI:P:131199)

A;Note: expression was shown in placenta, brain, heart, lung, liver, and kidney

R;von der Kammer, H.; Klaudiny, J.; Hanes, J.; Scheit, K.H.

submitted to the EMBL Data Library, April 1993

A;Description: The human homologue of the murine CDEI binding protein is an amyloid precursor like protein.

A;Reference number: S34644

A;Accession: S34644

A;Molecule type: mRNA

A;Residues: 1-763 <VON>

A;Cross-references: EMBL:Z22572; NID:g394763; PIDN:CAA80295.1; PID:g394764

R;Wasco, W.; Gurubhagavatula, S.; Paradis, M.; Romano, D.M.; Sisodia, S.S.;

Hyman, B.T.; Neve, R.L.; Tanzi, R.E.

Nature Genet. 5, 95-99, 1993

A;Title: Isolation and characterization of APLP2 encoding a homologue of the Alzheimer's associated amyloid beta protein precursor.

A;Reference number: S40519; MUID:94035131; PMID:8220435

A;Accession: S40519

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <WAS>

A;Cross-references: GB:L27631; NID:g450391; PIDN:AAC41701.1; PID:g450392

C;Genetics:

A;Gene: GDB:APLP2; APPL2

A;Cross-references: GDB:139159; OMIM:104776

A;Map position: 11q23-11q25

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; transmembrane protein

F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 47.2%; Score 1723; DB 2; Length 763;

Best Local Similarity 47.0%; Pred. No. 2.3e-83;

Matches 371; Conservative 112; Mismatches 166; Indels 140; Gaps 20;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | | | | | | | | | | : | | | | | | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFVAEAPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLYCQEMYPELQITNVMEANQVRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | | : | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | | | | | : : | : | | | : : | | | | : | | | | :
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTTES 282
      : | : | | : | | | : | | | | : : | | | | : : | | | | : |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLET PGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | | | : | | | | : | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | : | | | | | : | | | | | : | | | | | : | | | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL 470
      | | : | : | | | | | | | | | : | | | | | : | | | | | : | | | |
Db    485 RPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKT TVE 530
      | | | | | | | | | : | | | : | | | | : : | | | | : | | | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTN----- 585
      | : | | : : | : | | | | | | | | | : | | : : | | | :
Db    588 ---VSSEES-EEIPPFHPF--HPFPALPENE---DTQPELYHPM--KKGSGVGEQDGGL 635

Qy    586 IKTEE---ISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKG 625
      | | | | | : | : | | | : | : : : | | | | | : |
```

Db 636 IGAEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEEEERESVGPLREDFSLSSS 693

Qy 626 AIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENP 685  
|:|:|:| | | | | | |:|:|:|:|:|:| |:|:|:|:|:|:| |:|:|:|:|:|:|

Db 694 ALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENP 753

Qy 686 TYKFFEQMQ 694  
|:|:|:| | | | |

Db 754 TYKYLEQMQ 762

# RESULT 8

S42880

amyloid precursor-like protein - rat

C;Species: Rattus norvegicus (Norway rat)

C;Date: 06-Jan-1995 #sequence\_revision 06-Jan-1995 #text\_change 17-Mar-1999

C;Accession: S42880; S47528

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

submitted to the EMBL Data Library, March 1994

A;Description: Complete nucleotide and deduced amino acid sequence of rat amyloid precursor-like protein 2 (Aplp2/Apph): Two amino acids length difference to human and murine homologues.

A;Reference number: S42880

A;Accession: S42880

A;Molecule type: mRNA

A;Residues: 1-765 <SAN>

A;Cross-references: EMBL:X77934

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

Biochim. Biophys. Acta 1219, 167-170, 1994

A;Title: Complete nucleotide and deduced amino acid sequence of rat amyloid protein precursor-like protein 2 (APLP2/APPH): two amino acids length difference to human and murine homologues.

A;Reference number: S47528; MUID:94368849; PMID:8086458

A;Accession: S47528

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-765 <SA2>

A;Cross-references: EMBL:X77934

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing

F;312-362/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 46.8%; Score 1711; DB 2; Length 765;

Best Local Similarity 46.1%; Pred. No. 1e-82;

Matches 363; Conservative 122; Mismatches 167; Indels 136; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56  
|:|:|:| | | | | |:|:|:|:|:|:| |:|:|:|:|:|:| |:|:|:|:|:|:|

Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
:|:|:|:|:|:| |:|:|:|:|:|:|:|:|:|:|:|:| |:|:|:|:|:|:| |:|:|:|:|:|:|

Db 75 TGTKSCLGTKEEVLYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132

Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176  
|:|:|:|:|:|:| |:|:|:|:|:|:|:|:|:|:|:|:| |:|:|:|:|:|:| |:|:|:|:|:|:|





A;Title: Expression of a ubiquitous, cross-reactive homologue of the mouse beta-amyloid precursor protein (APP).  
A;Reference number: A49974; MUID:94132029; PMID:8300594  
A;Accession: A49974  
A;Status: preliminary; not compared with conceptual translation  
A;Molecule type: nucleic acid  
A;Residues: 1-751 <SLU>  
A;Cross-references: GB:U15571; NID:g558467; PIDN:AAA50603.1; PID:g558468  
A;Note: sequence extracted from NCBI backbone (NCBIP:144636)  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology  
F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 46.5%; Score 1699; DB 2; Length 751;  
Best Local Similarity 45.8%; Pred. No. 4.2e-82;  
Matches 362; Conservative 113; Mismatches 160; Indels 156; Gaps 20;

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Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | :|||  || | :          |||  :|||||||:||||:| | | : ||
Db      15 LLVLLLGLTAPAAALAGYIEALAANAGTGFVAEPEQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy      57 SGTKTCTIDTKEGILQYQCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      :|||:| : || :|||||:|||||||:||||| | :||:| :|||: | |||:
Db      75 TGTKSCLGTKEEVLQYQCQEIPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy     117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      ||||| |||| | : | ||||: || | |||: || | : | : |||||:
Db     133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSGMLLPCGV 192

Qy     177 DKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAE---E 231
      |:| | |:||| : :||: | : ||: | | || : : | |
Db     193 DQFHGTEYVCCPQTKTVDSSTMSKEEEEEEE-----DEEDEEEDYDLDKSEFPTE 243

Qy     232 EEVAEVEEEEEAD-DEDEDGDEVEEE-----AEPYEEATERTTSSIATTT 276
      :: : | || :||:|:|:| | : | | | :| | |
Db     244 ADLEDFTAAADEEEEEDEEEGEEVVEDRDYYYDPFKGDDYNEENPTSPSSEGTIS----- 298

Qy     277 TTTTESVEEV----- 286
      | | :|
Db     299 --DKEIVHDVKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNNFESEDYC 356

Qy     287 -----VRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 341
      :| | | | | | | | :||| | |||:| | :| | | :| :|||
Db     357 MAVCKAMIPPTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEA 415

Qy     342 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRRLALENY 401
      | ||||| : : :||| | :||:|:|:|:|:| |||||:|||||
Db     416 ELQAKNLPKTERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRRLALENY 475

Qy     402 ITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAQIRSQVMTHLRV 461
      : |||: ||| : | :||| || | ||:|:| | ||:||||:||||| |
Db     476 LAALQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHV 535

Qy     462 IYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNLMP 521
      | || ||||| || ||:|:|:|:|:|:| : | | |
Db     536 IEERRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTSS 578

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Qy      522 LTETKTTVELLPVNGEFSLDDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGS 581
          : : |      | :      | :      | | |      | : : | |
Db      579 ISENPVDVRVSSEESE-EIPPFHPLHPF-----PSLSENE-----GSGMAEQDG- 621

Qy      582 GLTNIKTEEI-SEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----N 623
          ||      : : | | : || |      |      : |      : : : | | | |      :
Db      622 GLIGAEKVIN SKNKMDENMVIDETLDV--KEMIFNAERVGGLEEEPE SVGPLREDFSL S 679

Qy      624 KGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHG VVEVDAAVTPEERHLSKMQQNGYE 683
          | : || : | | | || | | | : | : | : | : | : | | | | : | | | : | |
Db      680 SNALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQN HGYE 739

Qy      684 NPTYKFFEQMQ 694
          | | | | : | | |
Db      740 NPTYKYLEQMQ 750

```

# RESULT 10

A46362

amyloid precursor-like protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 21-Sep-1993 #sequence\_revision 18-Nov-1994 #text\_change 24-Nov-1999

C;Accession: A46362

R;Wasco, W.; Bupp, K.; Magendantz, M.; Gusella, J.F.; Tanzi, R.E.; Solomon, F.  
Proc. Natl. Acad. Sci. U.S.A. 89, 10758-10762, 1992

A;Title: Identification of a mouse brain cDNA that encodes a protein related to  
the Alzheimer disease-associated amyloid beta protein precursor.

A;Reference number: A46362; MUID:93066322; PMID:1279693

A;Accession: A46362

A;Status: preliminary

A;Molecule type: nucleic acid

A;Residues: 1-653 <WAS>

A;Experimental source: brain

A;Note: sequence inconsistent with the nucleotide translation

A;Note: sequence extracted from NCBI backbone (NCBIN:118683, NCBIP:118684)

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology

C;Keywords: transmembrane protein

Query Match 32.3%; Score 1180; DB 2; Length 653;

Best Local Similarity 38.4%; Pred. No. 7.4e-55;

Matches 269; Conservative 121; Mismatches 232; Indels 78; Gaps 17;

```

Qy      1 MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGT 59
          : | | : | | | | | | | | : |      | : | | | | : | : : | : | : | :
Db      22 LLP-LSLLLLRAQLAVGNLAVGSPSAAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS 80

Qy      60 KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL 118
          : | :      : : | : | : | | | | | | | | : | : | : | : | : | |
Db      81 RRCLLDLPQRVLEYCRQMPYELHIARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVPFHCL 140

Qy      119 VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK 178
          | | | | : | | | | : | : | | | | | | | : | : | | | : | : | | | | :
Db      141 PGEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQAEACSSQGLILHGSGMLLPCGSDR 200

Qy      179 FRGVEFVCCPLAEESDNVDSADAEEDDSVW-WGGADTDYADGSEDKVVEVAEEEEVAEV 237
          | | | | : | | | |      : |      | :      : | |      | : | | |      | | |

```

```

Db      201 FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF 248
Qy      238 EEEEADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP 297
      : | : :| ||| | : | : : | | ||
Db      249 PQPVDDYFVEPPQAEeeeeeeeeERAPPPSSHTPVMVSRVTPTPR-----PT----- 294
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
      | || | ||: || | :|| || : :||| || | :| ||||| ||: ||:
Db      295 DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN 354
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
      :||| :||:| : : |||:|||| || |:|:| || || :| || ||: |
Db      355 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPPQAERVLN 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:| |||||:|:|:|:| |||:| | |:| || |||:| | ||||| || |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRQVQVQTHLQVIEERMNQSLGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      :|:|: : : ||| || : : || :| | :| |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKM 596
      ||| |:::| | :| | : | : : :
Db      511 ----GSLQP-----PESKDDPPVTLTLP---KGSTDQESSSSGREKLTPLEQYEQ 551
Qy      597 DAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVML-KKKQ 652
      |: | |: |::| |::| :|:|:| |||
Db      552 KVNASAPRGFPFHSSDIQRDELAPSGTGVSRREALSGLLIMGAGGSLIVLSLLLLRKKKP 611
Qy      653 YTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      | :| ||||| :| ||: | :|:| |||||:| |:
Db      612 YGTISHGVVEVDPMLTLEEQLRELQRHGYENPTYRFLEE 651

```

# RESULT 11

JC1404

CDEI-box DNA-binding protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 30-Sep-1993 #sequence\_revision 30-Sep-1993 #text\_change 16-Feb-1997

C;Accession: JC1404

R;Vidal, F.; Blangy, A.; Rassoulzadegan, M.; Cuzin, F.

Biochem. Biophys. Res. Commun. 189, 1336-1341, 1992

A;Title: A murine sequence-specific DNA binding protein shows extensive local similarities to the amyloid precursor protein.

A;Reference number: JC1404; MUID:93129193; PMID:1482349

A;Accession: JC1404

A;Molecule type: mRNA

A;Residues: 1-511 <VID>

C;Comment: This protein plays an important role in the early development of the mouse.

C;Keywords: DNA binding; transmembrane protein

Query Match 31.2%; Score 1138; DB 2; Length 511;

Best Local Similarity 45.6%; Pred. No. 8.9e-53;

Matches 252; Conservative 92; Mismatches 129; Indels 80; Gaps 16;

Qy 174 CGIDKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAE- 230  
 |::|:| | |::| | : |:: | : |:: | | | | : : |  
 Db 6 CGVDQFHGTEYVCCPQTKTVSDSDSTMSKEEEEEEE-----DEEDEEDYDLKSEF 56

Qy 231 --EEEVAEVEEEEAD-DEDEDGDEVEEEAE-----EPYEEATERTTSIATTTTTT 279  
 | : : | | |::|:|:| | : : : | | | : : | :  
 Db 57 PTEADLEDFTEAAADEEEEEDEEGEEVVEDRDYYYDPFKGDDYNE--ENPTEPSSEGTIS 114

Qy 280 TESVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWE 339  
 : : |::| | | | | | | | |::| | | | | : | | : | : |  
 Db 115 DKEIVHDVKVPPTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNMRMDRVKKEWE 173

Qy 340 EAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALE 399  
 | | | | | | | : : : | | | | : | : | | | | | | | | | | : | |  
 Db 174 EAELQAKNLPKTERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRIALE 233

Qy 400 NYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHL 459  
 | : | | : | | | : | : | | | | | | | | : : | | | : | | | : | | | |  
 Db 234 NYLAALQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHL 293

Qy 460 RVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNLDM 519  
 | | | | | | | | | | | | : | : | : | : | : | : | : | : | : |  
 Db 294 HVIEERRNQSLSLLYKVFPYVAQEIQEEIDELLQEQR-----ADM-----DQFT 336

Qy 520 PSLTETKTTVELLPVNGEFLDDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRP 579  
 | : | | : | : | : | : | : | : | : | : | : | : | : | : | : |  
 Db 337 SSISENPVDVRSSEESE-EIPPFHPLHPF-----PSLSENE-----GSGMAEQD 380

Qy 580 GSGLTNIKTEEI-SEVKMDAEFRHDSGYEVHHQKLFFAEDVGS----- 622  
 | | | : : | | : | | : | : : | | | |  
 Db 381 G-GLIGAEKVINSKNKMMDENMVIDETLDV--KEMIFNAERVGGLEEEEPESVGPLREDFS 437

Qy 623 -NKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNG 681  
 : | : | : | | | | | : | : | : | : | : | : | : | : | : | : |  
 Db 438 LSSNALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHG 497

Qy 682 YENPTYKFFEQMQ 694  
 | | | | : | | |  
 Db 498 YENPTYKYLEQMQ 510

# RESULT 12

T15795

hypothetical protein C42D8.8 - *Caenorhabditis elegans*

C;Species: *Caenorhabditis elegans*

C;Date: 20-Sep-1999 #sequence\_revision 20-Sep-1999 #text\_change 01-Dec-2000

C;Accession: T15795; A49414

R;Hallsworth, K.

submitted to the EMBL Data Library, April 1996

A;Description: The sequence of *C. elegans* cosmid C42D8.

A;Reference number: Z18405

A;Accession: T15795

A;Status: preliminary; translated from GB/EMBL/DDBJ

A;Molecule type: DNA

A;Residues: 1-686 <HAL>

A;Cross-references: EMBL:U56966; NID:g1293844; PID:g1293850; PIDN:AAA98722.1;

GSPDB:GN00028; CESP:C42D8.8

A;Experimental source: strain Bristol N2; clone C42D8  
R;Daigle, I.; Li, C.  
Proc. Natl. Acad. Sci. U.S.A. 90, 12045-12049, 1993  
A;Title: apl-1, a *Caenorhabditis elegans* gene encoding a protein related to the human beta-amyloid protein precursor.  
A;Reference number: A49414; MUID:94089766; PMID:8265668  
A;Accession: A49414  
A;Status: preliminary  
A;Molecule type: mRNA  
A;Residues: 7-686 <DAI>  
A;Cross-references: GB:U00240; NID:g416296; PIDN:AAC46470.1; PID:g416297  
C;Genetics:  
A;Gene: CESP:C42D8.8  
A;Map position: X  
A;Introns: 22/3; 78/3; 121/1; 199/1; 230/1; 274/3; 344/3; 410/2; 471/2; 537/3; 580/3  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

```

Db      415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVPDISVE----DSELTPIIHDDFFSK 470
Qy      514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLPWHSFGADSV PANT---ENEVEP 564
      |  | : |  :  : : |  | : :  :  |  | : : |
Db      471 NAKLDVKAPTTTAKPVKETDNAKVLPTEASDSEEEADEYYEDEDDEQVKKTPDMKKKKVKV 530
Qy      565 VDARP-----AADRGLTTRPGSGLTNIKTEE-----ISEVKMDA 598
      || : |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Db      531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDDDDDSSSSSTSSESDDEDKNIKELRVDI 590
Qy      599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLK 649
      |  : : |  | : |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
Db      591 EPIIDEPASFYRHD-----KLIQSPEVERSAVSFQPYVLASAMFITAICIIFAIT 642
Qy      650 KKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
      :  | : : |  | : : |  | : : |  | : : |  | : : |  | : : |
Db      643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

```

# RESULT 13

A32758

beta-amyloid-like protein precursor - fruit fly (*Drosophila melanogaster*)

C;Species: *Drosophila melanogaster*

C;Date: 08-Dec-1989 #sequence\_revision 08-Dec-1989 #text\_change 24-Sep-1998

C;Accession: A32758

R;Rosen, D.R.; Martin-Morris, L.; Luo, L.; White, K.

Proc. Natl. Acad. Sci. U.S.A. 86, 2478-2482, 1989

A;Title: A *Drosophila* gene encoding a protein resembling the human beta-amyloid protein precursor.

A;Reference number: A32758; MUID:89184650; PMID:2494667

A;Accession: A32758

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-886 <ROS>

A;Cross-references: GB:J04516; NID:g158371; PID:g158372

C;Genetics:

A;Gene: FlyBase:Appl

A;Cross-references: FlyBase:FBgn0000108

C;Keywords: transmembrane protein

Query Match 20.6%; Score 754; DB 2; Length 886;

Best Local Similarity 25.7%; Pred. No. 2.9e-32;

Matches 234; Conservative 127; Mismatches 287; Indels 264; Gaps 29;

```

Qy      7 LLLLAAWTARALEVPTDGNAGLLA-----EPQIAMFC--GRLNMHMNV-QNGKWDSDPSG 58
      ||| : |  | :  | | : |  |||| : |  | :  :  : : | : | |
Db      9 LLLRSLWVVLAI-----GTAQVQAASPRWEPQIAVLCEAGQIQPYLSEEGRWVTDLSK 63
Qy      59 T---KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRG---RKQCKTHPHFV 112
      || : |  : | || : |  ||| : ||  ||| : || :  | || : |  : :
Db      64 KTTGPTCLRDKMDLLDYCKKAYPNRDITNIVESSHYQKIGGWCRQGALNAAKCKGSHRWI 123
Qy      113 IPYRCLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLL 172
      | : || |  | | |||| : |  |  |  |  |  : | :  | :  :  : |||
Db      124 KPFRCCL-GPFQSDALLVPEGCLFDHIHNASRCWPFVRWNQTGAAACQERGQMRTFAMLL 182
Qy      173 PCGIDKFRGVEFVCCP-----LAESDNVD---SA 199

```



C;Accession: S38344  
R;Hanes, J.; von der Kammer, H.; Kristjansson, G.I.; Scheit, K.H.  
Biochim. Biophys. Acta 1216, 154-156, 1993  
A;Title: The complete cDNA coding sequence for the mouse CDEI binding protein.  
A;Reference number: S38344; MUID:94032480; PMID:8218408  
A;Accession: S38344  
A;Status: preliminary  
A;Molecule type: mRNA  
A;Residues: 1-246 <HAN>  
A;Cross-references: EMBL:Z22592  
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type  
proteinase inhibitor homology

## RESULT 15

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)  
C;Species: Oryctolagus cuniculus (domestic rabbit)  
C;Date: 30-Sep-1993 #sequence\_revision 19-Oct-1995 #text\_change 19-Oct-1995  
C;Accession: PQ0438; C60045  
R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.  
Biochem. Biophys. Res. Commun. 188, 905-911, 1992  
A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.  
A;Reference number: PQ0438; MUID:93075180; PMID:1445331  
A;Accession: PQ0438  
A;Molecule type: DNA  
A;Residues: 1-82 <DAV>  
A;Cross-references: GB:M83558; GB:M83657  
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.  
Brain Res. Mol. Brain Res. 10, 299-305, 1991



A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157

A;Accession: C60045

A;Molecule type: mRNA

A;Residues: 12-68 <JOH>

A;Cross-references: EMBL:X56129

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

Query Match 11.1%; Score 406; DB 2; Length 82;  
Best Local Similarity 98.8%; Pred. No. 3.1e-15;  
Matches 81; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```
Qy      581 SGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 640
          |||
Db       1 SGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATV 60

Qy      641 IFITLVMLKKKQYTSIHGGVVE 662
          | |||
Db       61 IVITLVMLKKKQYTSIHGGVVE 82
```

Search completed: July 26, 2004, 12:47:29  
Job time : 15.6667 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:46:43 ; Search time 44.3333 Seconds  
(without alignments)  
4923.349 Million cell updates/sec

Title: US-09-806-194A-20  
Perfect score: 3653  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1288442 seqs, 313154207 residues

Total number of hits satisfying chosen parameters: 1288442

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Published Applications\_AA:\*

- 1: /cgn2\_6/ptodata/1/pubpaa/US07\_PUBCOMB.pep:\*
- 2: /cgn2\_6/ptodata/1/pubpaa/PCT\_NEW\_PUB.pep:\*
- 3: /cgn2\_6/ptodata/1/pubpaa/US06\_NEW\_PUB.pep:\*
- 4: /cgn2\_6/ptodata/1/pubpaa/US06\_PUBCOMB.pep:\*
- 5: /cgn2\_6/ptodata/1/pubpaa/US07\_NEW\_PUB.pep:\*
- 6: /cgn2\_6/ptodata/1/pubpaa/PCTUS\_PUBCOMB.pep:\*
- 7: /cgn2\_6/ptodata/1/pubpaa/US08\_NEW\_PUB.pep:\*
- 8: /cgn2\_6/ptodata/1/pubpaa/US08\_PUBCOMB.pep:\*
- 9: /cgn2\_6/ptodata/1/pubpaa/US09A\_PUBCOMB.pep:\*
- 10: /cgn2\_6/ptodata/1/pubpaa/US09B\_PUBCOMB.pep:\*
- 11: /cgn2\_6/ptodata/1/pubpaa/US09C\_PUBCOMB.pep:\*
- 12: /cgn2\_6/ptodata/1/pubpaa/US09\_NEW\_PUB.pep:\*
- 13: /cgn2\_6/ptodata/1/pubpaa/US10A\_PUBCOMB.pep:\*
- 14: /cgn2\_6/ptodata/1/pubpaa/US10B\_PUBCOMB.pep:\*
- 15: /cgn2\_6/ptodata/1/pubpaa/US10C\_PUBCOMB.pep:\*
- 16: /cgn2\_6/ptodata/1/pubpaa/US10\_NEW\_PUB.pep:\*
- 17: /cgn2\_6/ptodata/1/pubpaa/US60\_NEW\_PUB.pep:\*
- 18: /cgn2\_6/ptodata/1/pubpaa/US60\_PUBCOMB.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

		8				Query	
Result	No.	Score	Match	Length	DB	ID	Description

1	3653	100.0	697	9	US-09-794-927-20	Sequence 20, Appl
2	3653	100.0	697	9	US-09-795-847-20	Sequence 20, Appl
3	3653	100.0	697	9	US-09-794-743-20	Sequence 20, Appl
4	3653	100.0	697	9	US-09-794-748-20	Sequence 20, Appl
5	3653	100.0	697	9	US-09-794-925-20	Sequence 20, Appl
6	3653	100.0	697	9	US-09-681-442-20	Sequence 20, Appl
7	3653	100.0	697	10	US-09-869-414-20	Sequence 20, Appl
8	3653	100.0	697	10	US-09-548-366-20	Sequence 20, Appl
9	3653	100.0	697	12	US-10-652-927-20	Sequence 20, Appl
10	3653	100.0	697	12	US-10-652-830-20	Sequence 20, Appl
11	3646	99.8	697	9	US-09-794-927-16	Sequence 16, Appl
12	3646	99.8	697	9	US-09-795-847-16	Sequence 16, Appl
13	3646	99.8	697	9	US-09-794-743-16	Sequence 16, Appl
14	3646	99.8	697	9	US-09-794-748-16	Sequence 16, Appl
15	3646	99.8	697	9	US-09-794-925-16	Sequence 16, Appl
16	3646	99.8	697	9	US-09-681-442-16	Sequence 16, Appl
17	3646	99.8	697	10	US-09-869-414-16	Sequence 16, Appl
18	3646	99.8	697	10	US-09-548-366-16	Sequence 16, Appl
19	3646	99.8	697	12	US-10-652-927-16	Sequence 16, Appl
20	3646	99.8	697	12	US-10-652-830-16	Sequence 16, Appl
21	3643	99.7	695	9	US-09-794-927-14	Sequence 14, Appl
22	3643	99.7	695	9	US-09-795-847-14	Sequence 14, Appl
23	3643	99.7	695	9	US-09-794-743-14	Sequence 14, Appl
24	3643	99.7	695	9	US-09-794-748-14	Sequence 14, Appl
25	3643	99.7	695	9	US-09-794-925-14	Sequence 14, Appl
26	3643	99.7	695	9	US-09-681-442-14	Sequence 14, Appl
27	3643	99.7	695	10	US-09-869-414-14	Sequence 14, Appl
28	3643	99.7	695	10	US-09-548-366-14	Sequence 14, Appl
29	3643	99.7	695	12	US-10-652-927-14	Sequence 14, Appl
30	3643	99.7	695	12	US-10-652-830-14	Sequence 14, Appl
31	3638	99.6	697	9	US-09-794-927-18	Sequence 18, Appl
32	3638	99.6	697	9	US-09-795-847-18	Sequence 18, Appl
33	3638	99.6	697	9	US-09-794-743-18	Sequence 18, Appl
34	3638	99.6	697	9	US-09-794-748-18	Sequence 18, Appl
35	3638	99.6	697	9	US-09-794-925-18	Sequence 18, Appl
36	3638	99.6	697	9	US-09-681-442-18	Sequence 18, Appl
37	3638	99.6	697	10	US-09-869-414-18	Sequence 18, Appl
38	3638	99.6	697	10	US-09-548-366-18	Sequence 18, Appl
39	3638	99.6	697	12	US-10-652-927-18	Sequence 18, Appl
40	3638	99.6	697	12	US-10-652-830-18	Sequence 18, Appl
41	3636	99.5	695	9	US-09-794-927-10	Sequence 10, Appl
42	3636	99.5	695	9	US-09-795-847-10	Sequence 10, Appl
43	3636	99.5	695	9	US-09-794-743-10	Sequence 10, Appl
44	3636	99.5	695	9	US-09-794-748-10	Sequence 10, Appl
45	3636	99.5	695	9	US-09-794-925-10	Sequence 10, Appl

#### ALIGNMENTS

##### RESULT 1

US-09-794-927-20

; Sequence 20, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

```

; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 20
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-927-20

```

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Query Match          100.0%; Score 3653; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 2.5e-224;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
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Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
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Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

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Qy 361 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
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 Db 361 QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
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 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
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 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
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 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHD SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHG V 660  
 |||  
 Db 601 RHD SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHG V 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 2

US-09-795-847-20

; Sequence 20, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens  
US-09-795-847-20

Query Match 100.0%; Score 3653; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTTSVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTTTSVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVKMDAEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVKMDAEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
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Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
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RESULT 3

US-09-794-743-20  
; Sequence 20, Application US/09794743  
; Patent No. US20010021391A1  
; GENERAL INFORMATION:  
; APPLICANT: Gurney, Mark E.  
; APPLICANT: Bienkowski, Michael J.  
; APPLICANT: Heinrikson, Robert L.  
; APPLICANT: Parodi, Luis A.  
; APPLICANT: Yan, Riqiang  
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND  
; TITLE OF INVENTION: USES  
; TITLE OF INVENTION: THEREFOR  
; FILE REFERENCE: 28341/6280BC  
; CURRENT APPLICATION NUMBER: US/09/794,743  
; CURRENT FILING DATE: 2001-02-27  
; PRIOR APPLICATION NUMBER: 09/416,901  
; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 09/404,133  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-743-20

Query Match 100.0%; Score 3653; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360  
 |||||  
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
 |||||  
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
 |||||  
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
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 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660  
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 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697  
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 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

#### RESULT 4

US-09-794-748-20

; Sequence 20, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24



; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-20

Query Match 100.0%; Score 3653; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60
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Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60

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Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
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Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
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Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
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Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
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Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660
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Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
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Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 5

US-09-794-925-20

; Sequence 20, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-20

Query Match 100.0%; Score 3653; DB 9; Length 697;

Best Local Similarity 100.0%; Pred. No. 2.5e-224;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGK 60

Qy     61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPQLITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
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 Db 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300  
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 Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360  
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 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360  
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 Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||||  
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
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 Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
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 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480  
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 Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540  
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 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540  
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 Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
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 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
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 Db 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMKKKQYTSIHHGV 660  
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 Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||||  
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
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RESULT 6

US-09-681-442-20

; Sequence 20, Application US/09681442

; Patent No. US20020081634A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/681,442

; CURRENT FILING DATE: 2001-04-05

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-681-442-20

Query Match 100.0%; Score 3653; DB 9; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660



Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 8

US-09-548-366-20

; Sequence 20, Application US/09548366

; Publication No. US20030104365A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND

; TITLE OF INVENTION: USES THEREFOR

; FILE REFERENCE: 28341/6280A

; CURRENT APPLICATION NUMBER: US/09/548,366

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 65  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-548-366-20

Query Match 100.0%; Score 3653; DB 10; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAI IGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAI IGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 9

US-10-652-927-20

; Sequence 20, Application US/10652927

; Publication No. US20040043408A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N3

; CURRENT APPLICATION NUMBER: US/10/652,927

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver.. 2.0

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-10-652-927-20

Query Match 100.0%; Score 3653; DB 12; Length 697;

Best Local Similarity 100.0%; Pred. No. 2.5e-224;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
|  
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120  
|  
Db 61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
|  
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240  
|  
Db 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300



Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 10

US-10-652-830-20

; Sequence 20, Application US/10652830

; Publication No. US20040048303A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N1

; CURRENT APPLICATION NUMBER: US/10/652,830

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 20  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-10-652-830-20

Query Match 100.0%; Score 3653; DB 12; Length 697;  
Best Local Similarity 100.0%; Pred. No. 2.5e-224;  
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
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## RESULT 11

US-09-794-927-16

; Sequence 16, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/794,927

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-927-16

Query Match 99.8%; Score 3646; DB 9; Length 697;

Best Local Similarity 99.9%; Pred. No. 7.1e-224;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
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Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Db	601	RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 12

US-09-795-847-16

; Sequence 16, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23



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Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697
Db      661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMKNKK 697

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RESULT 13

US-09-794-743-16

; Sequence 16, Application US/09794743

; Patent No. US20010021391A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280BC

; CURRENT APPLICATION NUMBER: US/09/794,743

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-743-16

Query Match 99.8%; Score 3646; DB 9; Length 697;

Best Local Similarity 99.9%; Pred. No. 7.1e-224;

Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Db      61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

```

Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240  
 |||

Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTTSVEEVVRVPTTAASTPDAV 300  
 |||

Db 241 EADDDDEDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTTTSVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360  
 |||

Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420  
 |||

Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480  
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540  
 |||

Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600  
 |||

Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITL VMLKKKQYTSIHHGV 660  
 |||

Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697  
 |||

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 14

US-09-794-748-16

; Sequence 16, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,  
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13  
; PRIOR APPLICATION NUMBER: 60/155,493  
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; PRIOR APPLICATION NUMBER: 09/404,133  
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; PRIOR APPLICATION NUMBER: PCT/US99/20881  
; PRIOR FILING DATE: 1999-09-23  
; PRIOR APPLICATION NUMBER: 60/101,594  
; PRIOR FILING DATE: 1998-09-24  
; NUMBER OF SEQ ID NOS: 73  
; SOFTWARE: PatentIn Ver. 2.0  
; SEQ ID NO 16  
; LENGTH: 697  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-09-794-748-16

Query Match 99.8%; Score 3646; DB 9; Length 697;  
Best Local Similarity 99.9%; Pred. No. 7.1e-224;  
Matches 696; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540





Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

Search completed: July 26, 2004, 13:00:45  
 Job time : 46.3333 secs

GenCore version 5.1.6  
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OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:53 ; Search time 35.3333 Seconds  
(without alignments)  
6224.043 Million cell updates/sec

Title: US-09-806-194A-20  
Perfect score: 3653  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1017041 seqs, 315518202 residues

Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SPTREMBL\_25:\*  
1: sp\_archaea:\*  
2: sp\_bacteria:\*  
3: sp\_fungi:\*  
4: sp\_human:\*  
5: sp\_invertebrate:\*  
6: sp\_mammal:\*  
7: sp\_mhc:\*  
8: sp\_organelle:\*  
9: sp\_phage:\*  
10: sp\_plant:\*  
11: sp\_rodent:\*  
12: sp\_virus:\*  
13: sp\_vertibrate:\*  
14: sp\_unclassified:\*  
15: sp\_rvirus:\*  
16: sp\_bacteriap:\*  
17: sp\_archeap:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

SUMMARIES

Result	Query					
No.	Score	Match	Length	DB	ID	Description
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1	3423	93.7	695	13	Q9DGJ8	Q9dgj8 gallus gall
2	3382	92.6	751	13	Q9DGJ7	Q9dgj7 gallus gall
3	3209	87.8	693	13	Q98SG0	Q98sg0 xenopus lae
4	3185	87.2	695	13	Q98SF9	Q98sf9 xenopus lae
5	3183	87.1	695	13	Q7ZXQ0	Q7zxq0 xenopus lae
6	3098	84.8	747	13	Q91963	Q91963 xenopus. ap
7	2959.5	81.0	699	13	O57394	O57394 narke japon
8	2762.5	75.6	569	13	Q9PVL1	Q9pvl1 gallus gall
9	2608	71.4	534	13	O93296	O93296 gallus gall
10	2562	70.1	678	13	Q7ZZT1	Q7zzt1 brachydanio
11	2524	69.1	738	13	Q90W28	Q90w28 brachydanio
12	2482.5	68.0	694	13	Q8UUR9	Q8uur9 brachydanio
13	2334	63.9	612	13	Q9I9E7	Q9i9e7 brachydanio
14	1923	52.6	384	11	Q8BPC7	Q8bpc7 mus musculu
15	1757	48.1	695	4	Q13861	Q13861 homo sapien
16	1744.5	47.8	669	4	Q14662	Q14662 homo sapien
17	1739	47.6	707	11	Q80US7	Q80us7 mus musculu
18	1735	47.5	695	11	Q64348	Q64348 mus musculu
19	1726	47.2	715	11	Q7TT34	Q7tt34 mus musculu
20	1703	46.6	763	11	Q61482	Q61482 mus musculu
21	1699	46.5	751	11	Q60709	Q60709 mus musculu
22	1650	45.2	472	13	Q8UUS0	Q8uus0 brachydanio
23	1345.5	36.8	357	13	Q8UUI8	Q8uui8 brachydanio
24	1296.5	35.5	522	4	Q9BT36	Q9bt36 homo sapien
25	1085	29.7	218	11	Q8BPV5	Q8bpv5 mus musculu
26	1043.5	28.6	523	4	Q14594	Q14594 homo sapien
27	790	21.6	357	13	Q7ZZT2	Q7zzt2 brachydanio
28	766	21.0	239	13	Q8UUI7	Q8uui7 brachydanio
29	572	15.7	113	13	Q8JH58	Q8jh58 chelydra se
30	561	15.4	182	11	Q9CYS4	Q9cys4 mus musculu
31	478	13.1	97	6	Q28673	Q28673 oryctolagus
32	435.5	11.9	140	13	Q800X9	Q800x9 chelydra se
33	396.5	10.9	82	4	Q16014	Q16014 homo sapien
34	390.5	10.7	82	4	Q16019	Q16019 homo sapien
35	387.5	10.6	82	4	Q16020	Q16020 homo sapien
36	371	10.2	79	11	O35463	O35463 cricetulus
37	358.5	9.8	160	11	Q9QZ78	Q9qz78 cavia sp. p
38	330	9.0	208	11	Q8R0R7	Q8r0r7 mus musculu
39	234	6.4	49	6	O97917	O97917 bos taurus
40	196.5	5.4	727	5	Q95TG7	Q95tg7 drosophila
41	196.5	5.4	5303	5	Q9V628	Q9v628 drosophila
42	192.5	5.3	556	5	Q95S93	Q95s93 drosophila
43	192.5	5.3	1110	13	Q91255	Q91255 petromyzon
44	191.5	5.2	556	5	Q9V7I9	Q9v7i9 drosophila
45	188	5.1	785	5	Q9GQ82	Q9gq82 drosophila

#### ALIGNMENTS

##### RESULT 1

Q9DGJ8

ID	Q9DGJ8	PRELIMINARY;	PRT;	695 AA.
AC	Q9DGJ8;			
DT	01-MAR-2001	(TrEMBLrel. 16, Created)		
DT	01-MAR-2001	(TrEMBLrel. 16, Last sequence update)		
DT	01-JUN-2003	(TrEMBLrel. 24, Last annotation update)		



Qy 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA 478  
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 Db 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSFLYNVPA 478  
 Qy 479 VAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEF 538  
 |||:|  
 Db 479 VAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVDGEF 538  
 Qy 539 SLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDA 598  
 |||:|:|  
 Db 539 SLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTEE VSEVKMDA 598  
 Qy 599 EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHH 658  
 |||  
 Db 599 EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHH 658  
 Qy 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695  
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 Db 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN 695

# RESULT 2

Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.  
 AC Q9DGJ7;  
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)  
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein 751 isoform.  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Sarasa M., Rodolosse A., Sorribas V.;  
 RT "Cloning of full-length chicken beta-amyloid precursor protein  
 RT isoforms."  
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AF289219; AAG00594.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.



Db 659 DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVE 718

Qy 663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 695  
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Db 719 VDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 751

# RESULT 3

Q98SG0

ID Q98SG0 PRELIMINARY; PRT; 693 AA.  
 AC Q98SG0;  
 DT 01-JUN-2001 (TrEMBLrel. 17, Created)  
 DT 01-JUN-2001 (TrEMBLrel. 17, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Beta-amyloid precursor protein A.  
 GN APP.  
 OS Xenopus laevis (African clawed frog).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;  
 OC Xenopodinae; Xenopus.  
 OX NCBI\_TaxID=8355;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Van den Hurk W.H.;  
 RL Thesis (2001), Department of Biological Sciences,  
 RL University of Nijmegen, Nijmegen, Netherlands.  
 DR EMBL; AJ298150; CAC37193.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Signal.  
 FT SIGNAL 1 18 POTENTIAL.  
 SQ SEQUENCE 693 AA; 78568 MW; CAF1DF655C1AB653 CRC64;

Query Match 87.8%; Score 3209; DB 13; Length 693;  
 Best Local Similarity 87.7%; Pred. No. 1.2e-185;  
 Matches 611; Conservative 36; Mismatches 44; Indels 6; Gaps 4;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK 60  
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Db 1 MLPHITLLVLTIV-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVSGK 59

Qy 61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120  
 || ||||| : ||||| : ||| : |||||

Db 60 GCIGTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG 119

Qy 121 EFVSDALLVPDKCKFLHQERMDVCEHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 ||||| : ||||| : |||| : ||| : |||||

Db 120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKSMLEHYGMLLPCGIDKFR 179



Qy	181	GVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSSEDKVVEVA--EEEEVAEVE	238
Db	180	GVEFVCCPSAEESSEFDSADA-EDDSDAWWGGADADYVDRSDDKAVEAQPDEEEEVVEVE	238
Qy	239	EEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTTSESVEEVVRVPTTAASTPD	298
Db	239	EEETDDDED--DGDEAEPEPEPEYEEATERTTSIATTTTTTTTSESVEEVVRVPATAASTPD	296
Qy	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQ	358
Db	297	AVDKYLENPNDENEHDFLAKAKERLEGKHREKMSEVMKEWEEAERQAKNLPKADKKAVIQ	356
Qy	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNM	418
Db	357	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNM	416
Qy	419	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA	478
Db	417	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPA	476
Qy	479	VAEEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEF	538
Db	477	VAEEIQDEVDELFOKEQNYSDDMVSNMVS DHRVSYGNDALMPSLSETKTTVELLPVDGEF	536
Qy	539	SLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDA	598
Db	537	NIEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDS	596
Qy	599	EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHH	658
Db	597	EYRHDTAYEVHHQKLVFFAEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHH	656
Qy	659	GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	657	GVVEVDAAVTPEERHLTKMOONGYENPTYKFFEMON	693

DR EMBL; AJ298151; CAC37194.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Signal.  
 FT SIGNAL 1 18 POTENTIAL.  
 SQ SEQUENCE 695 AA; 78803 MW; DC14EB02AFB0204A CRC64;

Query Match 87.2%; Score 3185; DB 13; Length 695;  
 Best Local Similarity 87.1%; Pred. No. 3.5e-184;  
 Matches 608; Conservative 39; Mismatches 45; Indels 6; Gaps 5;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	60
		:	
Db	1	MLPHITLLVLTALGALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVS	59
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCL	120
Db	60	GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKSRTHIVVPIPYRCL	119
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	120	EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR	179
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEV--AEVEEVAEVE	238
Db	180	GVEFVCCPTAEESFDSADA-EDSDVWWGGADADYVDRSDDKAVEAQPEEEVEVEVE	238
Qy	239	EEEADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR-VPTTA	297
Db	239	EEEADDD-DEDDGDETEEEPEPEYEEATERTTTSIATTTTTTTESVEEVVRVAVPAT	297
Qy	298	DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVI	357
Db	298	DAVDKYLENPNDENEHDFLKAERLEKGRHREKMSQVMKEWEEAERQAKNLPKADKKAVI	357
Qy	358	QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVF	417
Db	358	QHFQEKVESLEQEAANERQQLVETHMARVEATLNDRRRIALENYITALQADPPRPRHVF	417
Qy	418	MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYN	477
Db	418	MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYK	477
Qy	478	AVAEIQDEVDLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGE	537
Db	478	AVAEIQDEVDLQKEQNYSDVMVSNMVSDFRVSYGNDAIMPSTETKTTVELLPVDGE	537
Qy	538	FSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD	597

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Db      538 FNVEDLQPWHSFGVDSVPANTENEVEPVDPARPAADRGLTTRPGSGLTNIKREEISEVKMD 597
Qy      598 AEFRHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMMLKKKQYTSIH 657
       :|:||: |||||:|||||:|:||||| | |||||:|
Db      598 SEYRHDAAYEVHHQKLFFFADEVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTTHI 657
Qy      658 HGVVEVDAAVTPEERHL SKMQONGYENPTYKFFEOMQN 695
       |||||:|||||
Db      658 HGVVEVDAAVTPEERHLTKMOONGYENPTYKFFEOMON 695

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## RESULT 5

07ZX00

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ID      Q7ZXQ0                                PRELIMINARY;          PRT;    695 AA.
AC      Q7ZXQ0;
DT      01-JUN-2003 (TrEMBLrel. 24, Created)
DT      01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT      01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE      Hypothetical protein.
OS      Xenopus laevis (African clawed frog).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Amphibia; Batrachia; Anura; Mesobatrachia; Pipioidea; Pipidae;
OC      Xenopodinae; Xenopus.
OX      NCBI_TaxID=8355;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Embryo;
RA      Klein S., Strausberg R.;
RL      Submitted (JAN-2003) to the EMBL/GenBank/DDBJ databases.
DR      EMBL; BC044324; AAH44324.1; -.
DR      GO; GO:0016020; C:membrane; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
KW      Hypothetical protein.
SQ      SEQUENCE      695 AA: 78803 MW: C1BD8AACC3356B05 CRC64;

```

Query Match 87.1%; Score 3183; DB 13; Length 695;  
Best Local Similarity 87.1%; Pred. No. 4.6e-184;  
Matches 608; Conservative 38; Mismatches 46; Indels 6; Gaps 5;

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Qy      1  MLPGIALLLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGR LNMH MNVQNGKWDSDPSGTK 60
      ||| : ||: | | | |||| ||| ||||| ||||| : ||||| ||||| : |||
Db      1  MLPHITLLVLTA-GALALEVPADGNGGLAEPQIAMFCGK LNMH MNVQNGKWETDVSGTK 59

Qy     61  TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || ||||| ||||| ||||| ||||| ||||| ||||| : ||||| : | |: |||||
Db     60  GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG .119

Qy    121  EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

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Db      120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR 179
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEV--AEEEEVAEVE 238
        |||||  ||||:  ||||  |||||  ||  |  |:|  ||  ||||  |||
Db      180 GVEFVCCPTAESESFDSADA-EDSDVWVGADADYVDRSDDKAVEAQPEEEEEVVEVE 238
Qy      239 EEEADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVR-VPTTAASTP 297
        |||||  ||:|  |||  |||||  |||||  |||||  |||||  ||  ||  |||
Db      239 EEEADDD-DDDDGDETEEEPEEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPATAVSTP 297
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
        |||||  |  ||||  |  |||||  ||||:  ||:  ||:  |||||  |||||  |||
Db      298 DAVDKYLENPNDENEHDFLKAKEERLEGGHREKMSQVMKEWEAAERQAKNLPKADKKAVI 357
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      358 QHFQEKVESLEQEAAKERQQLVETHMARVEATLNDRRRIALENYITALQADPPRPRHVFN 417
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
        |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP 477
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGE 537
        |||||  |||||  |||||  ||||:  ||:  ||:  |:  |||||  |||||  |||
Db      478 AVAEEIQDEVDELQKEQNYSDVMVSNMVSDFRVSYGNLMPSLSETKTTVELLPVDGE 537
Qy      538 FSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD 597
        |:  |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||
Db      538 FNVEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKREEISEVKMD 597
Qy      598 AEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH 657
        |:  |||:  |||||  ||||:  ||:  ||:  |:  |||||  |||||  |||
Db      598 SEYRHDAAYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIH 657
Qy      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        |||||  ||||:  |||||  |||||  |||||
Db      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

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# RESULT 6

Q91963

ID Q91963 PRELIMINARY; PRT; 747 AA.

AC Q91963;

DT 01-NOV-1996 (TrEMBLrel. 01, Created)

DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)

DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE APP747.

GN APP747.

OS Xenopus.

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;

OC Xenopodinae.

OX NCBI\_TaxID=8353;

RN [1]

RP SEQUENCE FROM N.A.

RX MEDLINE=93129227; PubMed=1282805;

RA Okado H., Okamoto H.;  
 RT "A Xenopus homologue of the human beta-amyloid precursor protein:  
 RT developmental regulation of its gene expression.";  
 RL Biochem. Biophys. Res. Commun. 189:1561-1568(1992).  
 DR EMBL; S52417; AAB24853.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Protease inhibitor; Serine protease inhibitor.  
 SQ SEQUENCE 747 AA; 84893 MW; A75E81885681D948 CRC64;

Query Match 84.8%; Score 3098; DB 13; Length 747;  
 Best Local Similarity 80.9%; Pred. No. 6.9e-179;  
 Matches 597; Conservative 35; Mismatches 42; Indels 64; Gaps 5;

Qy	17	ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWDSDPSGTKTCIDTKEGILQYCQE	75
Db	15	ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE	71
Qy	76	VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF	135
Db	72	VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF	131
Qy	136	LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEEEDN	195
Db	132	LHQERMDICETHLHWHTVAKESCSEKSMSLHEYGMLLPCGIDKFRGVEFVCCPSAEESES	191
Qy	196	VDSADAEEDSDVWVGADTDYADGSEDKVVEVA---EEEEVAEVEEEEADDDDEDGDE	253
		:	
Db	192	FDSADAAEDDCDVWVGADADYVDRSDDKAVEAQPDEEEVVEVEEEEETDDDED--DGDE	249
Qy	254	VEEEAEEPVEEATERTTSIATTTTTTTTSESVEEVVR-----	288
Db	250	AEEPEEPVEEATERTTSIATTTTTTTTSESVEEVVREVCSEAETGPCRAMISRWYYDVTE	309
Qy	289	-----VPTTAASTPDAVDKYLETPGDENEHAHFQ	317
		:	
Db	310	SKCAQFIYGGCGGNRNNFESDDYCMVCGSVIPATAASTPDAVDKYLENPDENEHDFL	369
Qy	318	KAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQ	377
Db	370	KAKERLEGKHREKMSEVMKEWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAKQRQQ	429

Qy 378 LVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHf 437  
 |||||:|||||  
 Db 430 LVETHMARVEAMLNDRRLALENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKHf 489  
 Qy 438 EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEQDEVELLQKEQNY 497  
 |||||  
 Db 490 EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPAAVEEQDEVELFQKEQNY 549  
 Qy 498 SDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSVPAN 557  
 |||::||:|:|:|||||:|||||:|||::|||  
 Db 550 SDDMVSNMVSDHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLQPWHSFGVDSVPAN 609  
 Qy 558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFA 617  
 |||||:|:|:|:|  
 Db 610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA 669  
 Qy 618 EDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKM 677  
 |:|||||:|||||:|||||:|||||:|  
 Db 670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGVEVDAAVTPEERHLTKM 729  
 Qy 678 QQNGYENPTYKFFEQQMN 695  
 |||||  
 Db 730 QQNGYENPTYKFFEQQMN 747

# RESULT 7

O57394

ID O57394 PRELIMINARY; PRT; 699 AA.  
 AC O57394;  
 DT 01-JUN-1998 (TrEMBLrel. 06, Created)  
 DT 01-JUN-1998 (TrEMBLrel. 06, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE EL amyloid precursor protein 699.  
 GN EL APP699.  
 OS Narke japonica (Electric ray).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Chondrichthyes;  
 OC Elasmobranchii; Squalia; Hypnosqualia; Pristiorajia; Batoidea;  
 OC Torpediniformes; Narcinoidei; Narkidae; Narke.  
 OX NCBI\_TaxID=62965;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Electric lobe;  
 RX MEDLINE=98129705; PubMed=9461486;  
 RA Iijima K., Lee D.-S., Okutsu J., Tomita S., Hirashima N., Kirino Y.,  
 RA Suzuki T.;  
 RT "cDNA isolation of Alzheimer's amyloid precursor protein from  
 RT cholinergic nerve terminals of the electric organ of the electric  
 RT ray."  
 RL Biochem. J. 330:29-33(1998).  
 DR EMBL; AB005544; BAA24230.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.



O9PVL1

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ID      Q9PVL1      PRELIMINARY;      PRT;      569 AA.
AC      Q9PVL1;
DT      01-MAY-2000 (TrEMBLrel. 13, Created)
DT      01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid protein (Fragment).
GN      APP.
OS      Gallus gallus (Chicken).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC      Gallus.
OX      NCBI_TaxID=9031;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Brain;
RA      Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT      "What the evolution of the amyloid protein precursor supergene family
RT      tells us about its function.";
RL      Neurochem. Int. 0:0-0(2000).
DR      EMBL; AF030341; AAF12698.1; -.
DR      HSSP; P05067; 1BA4.
DR      GO; GO:0016020; C:membrane; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER      1      1
SQ      SEQUENCE      569 AA;      64753 MW;      0AB8BB851863A19D CRC64;

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Query Match 75.6%; Score 2762.5; DB 13; Length 569;  
Best Local Similarity 93.4%; Pred. No. 8.9e-159;  
Matches 534; Conservative 14; Mismatches 19; Indels 5; Gaps 4;

Qy	126	ALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFV	185
		:	
Db	1	ALLVPDKCKLLHQERMDVCETHLHWHTVAKESCSEKSMNLHDYGMLLSCGIDKFRGVEFV	60
Qy	186	CCPLAEESDNVDSADAEEDDSDVWGGADTDYADGSEDKVVE--VAEEEEVAEEEEEEAD	243
		:     :             :      ::   ::	
Db	61	CCPLAEESDNLDSADAEDDDSDVWGGADADYADGSDDKVVEEQPEEDEELTVVEDEDAD	120
Qy	244	DDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAVDKY	303
		:    :	
Db	121	DD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDVVDKY	178
Qy	304	LETPGDENEHAHFQKAKERLEAKHREMSQVMREWEAAERQAKNLPKADKKAVIQHFQEK	363
Db	179	LETPGDENEHAHFQKAKERLEAKHREMSQVMREWEAAEROAKNLPKADKKAVIQHFOEK	238



QY 364 VESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYV 423  
 |||:|||||  
 Db 239 VESLEQEAAANERQQLVETHMARVEAMLNDRRIAENYITALQTVPPRPRHVFNMLKKYV 298  
 QY 424 RAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVAEEI 483  
 |||:|||||  
 Db 299 RAEQKDRQHTLKHFEHVRMVDPKKAVQIRSQVMTHLRVIYERMNQSLFLYNVPVAEEI 358  
 QY 484 QDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLDDL 543  
 |||:|||||  
 Db 359 QDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPTLTETKTTVELLPVVGESLDDL 418  
 QY 544 QPWSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHD 603  
 |||||:|||||  
 Db 419 QPWHFPGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTTEEVEVKMDAEFRHD 478  
 QY 604 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGVEV 663  
 |||:|||||  
 Db 479 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIANVIVITLVMLKKKQYTSIHGVEV 538  
 QY 664 DAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 695  
 |||||  
 Db 539 DAAVTP-ERHLSKMQQNGYENPTYKFFEQQMN 569

RESULT 9

O93296

ID O93296 PRELIMINARY; PRT; 534 AA.  
 AC O93296;  
 DT 01-NOV-1998 (TrEMBLrel. 08, Created)  
 DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)  
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
 DE Amyloid protein (Fragment).  
 OS Gallus gallus (Chicken).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
 OC Gallus.  
 OX NCBI\_TaxID=9031;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98337885; PubMed=9671674;  
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,  
 RA Milligan C.E.;  
 RT "Increased production of amyloid precursor protein provides a  
 RT substrate for caspase-3 in dying motoneurons."  
 RL J. Neurosci. 18:5869-5880(1998).  
 DR EMBL; AF042098; AAC25052.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.  
FT NON\_TER 1 1  
SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 71.4%; Score 2608; DB 13; Length 534;  
Best Local Similarity 94.6%; Pred. No. 1.8e-149;  
Matches 505; Conservative 13; Mismatches 12; Indels 4; Gaps 3;

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Qy      164 NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSED 223
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      3  NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNLDSADAEDDDSDVWWGGADADYADGSDD 62

Qy      224 KVVE--VAEEEEVAEVEEEEADDDDEDEDGDEVEEEAEOPYEEATERTTSIATTTTTTTE 281
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      63 KVVEEQPEEDEELTVVEDEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTE 120

Qy      282 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 341
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      121 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 180

Qy      342 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENY 401
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      181 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRIALENY 240

Qy      402 ITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 461
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      241 ITALQTVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 300

Qy      462 IYERMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPS 521
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      301 IYERMNQSLSFLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPS 360

Qy      522 LTETKTTVELLPVNGEFLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGS 581
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      361 LTETKTTVELLPVDGEFLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGS 420

Qy      582 GLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 641
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      421 GLTNVKTTEEVSVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 480

Qy      642 FITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      481 VITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 534
```

RESULT 10

Q7ZZT1

ID Q7ZZT1 PRELIMINARY; PRT; 678 AA.

AC Q7ZZT1;

DT 01-JUN-2003 (TrEMBLrel. 24, Created)

DT 01-JUN-2003 (TrEMBLrel. 24, Last sequence update)

DT 01-OCT-2003 (TrEMBLrel. 25, Last annotation update)

DE Amyloid protein a variant 2.

GN APPA.

OS Brachydanio rerio (Zebrafish) (Danio rerio).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;

OC Cyprinidae; Danio.  
 OX NCBI\_TaxID=7955;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Groth C., Lardelli M.;  
 RT "Investigation of zebrafish appa expression during embryogenesis."  
 RL Submitted (APR-2003) to the EMBL/GenBank/DDBJ databases.  
 DR EMBL; AY271746; AAP22958.1; -.  
 DR GO; GO:0016020; C:membrane; IEA.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 SQ SEQUENCE 678 AA; 76755 MW; 94163778444FD0BC CRC64;

Query Match 70.1%; Score 2562; DB 13; Length 678;  
 Best Local Similarity 71.9%; Pred. No. 1.5e-146;  
 Matches 498; Conservative 78; Mismatches 95; Indels 22; Gaps 11;

Qy	5	LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID	64
		:  :  :  :  :          :   : : : :       : :	
Db	6	LFILLMAVASTLAVEVPSDSGTGLLAEPQIAMFCGKLNMHINIQSGKWEPPDPSGSKSCIG	65
Qy	65	TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVGEFVS	124
		:  :  :    :      :	
Db	66	NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPIYRCLVGEFVS	125
Qy	125	DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF	184
		:  : :        :  :        :	
Db	126	DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF	185
Qy	185	VCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEEEEEADD	244
		: :           :    :   : :     :  :	
Db	186	VCCP-ADAGKESESAAVEEDDSVWVGAEADYTENSMTR--DAAAEPAV--LEDDEDAD	240
Qy	245	DEDDDEDGD-EVEEEAEPEYEEATERTT-SIATTTTTTTESVEEVVRVPTTAASTPDAVDK	302
		: :     : : :         :   : : :       :       :	
Db	241	EEDEDEDGDGRDEKIEEEEEERTQSTSAALTSTTTTTTESVEEVVRVPTPSSSPDAVDR	300
Qy	303	YLETPGDENENAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQE	362
		:  :	
Db	301	YLETPADENENAHFLKAKESLETKHRERMSQVMREWEAERQAKSLPRNDKKAVIQHFQE	360
Qy	363	KVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKY	422
		:    : :      :   :      :  :        :	
Db	361	KVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLLKKY	420
Qy	423	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVAEE	482
		:  :                        :	
Db	421	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSLGLLYKVPGVADD	480
Qy	483	IQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDD	542

Db	481	IQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDALMPDST---AGLELLPAEDTQGGFGF	536
Qy	543	LQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRH	602
Db	537	IHP-ESFN----QPNTHNQVEPVDARVPDLDLATRPVSGL---KPDDIPELRMEAEERH	588
Qy	603	DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGVVE	662
Db	589	S---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIVITLVMLRKKQYTSIHGGIIE	645
Qy	663	VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	646	VDAAVTPEERHLSKMOONGYENPTYKFFEOMHN	678

Q90W28

```

ID      Q90W28      PRELIMINARY;      PRT;      738 AA.
AC      Q90W28;
DT      01-DEC-2001 (TrEMBLrel. 19, Created)
DT      01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid precursor protein.
GN      APPA OR APP.
OS      Brachydanio rerio (Zebrafish) (Danio rerio).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC      Cyprinidae; Danio.
OX      NCBI_TaxID=7955;
RN      [1]
RP      SEQUENCE FROM N.A.
RA      Groth C., Lardelli M.;
RT      "Expression analysis of zebrafish app.";
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
DR      EMBL; AF389401; AAK64495.1; -.
DR      ZFIN; ZDB-GENE-000616-13; appa.
DR      GO; GO:0016020; C:membrane; IEA.
DR      GO; GO:0004867; F:serine protease inhibitor activity; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      InterPro; IPR002223; Kunitz_BPTI.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      Pfam; PF00014; Kunitz_BPTI; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PRINTS; PR00759; BASICPTASE.
DR      ProDom; PD000222; Kunitz_BPTI; 1.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      SMART; SM00131; KU; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
DR      PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR      PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW      Protease inhibitor; Serine protease inhibitor.
SQ      SEQUENCE      738 AA;  83577 MW;  AF480F6D308FD298 CRC64;

```



# RESULT 12

Q8UUR9

ID Q8UUR9 PRELIMINARY; PRT; 694 AA.  
AC Q8UUR9;  
DT 01-MAR-2002 (TrEMBLrel. 20, Created)  
DT 01-MAR-2002 (TrEMBLrel. 20, Last sequence update)  
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)  
DE Putative membrane protein.  
GN APPB.  
OS Brachydanio rerio (Zebrafish) (Danio rerio).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;  
OC Cyprinidae; Danio.  
OX NCBI\_TaxID=7955;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Brain;  
RX PubMed=11862463;  
RA Musa A., Lehrach H., Russo V.E.A.;  
RT "Distinct expression patterns of two zebrafish homologues of the human  
RT APP gene during embryonic development.";  
RL Dev. Genes Evol. 211:563-567(2001).  
DR EMBL; AJ315639; CAC85736.1; -.  
DR ZFIN; ZDB-GENE-020220-1; appb.  
DR GO; GO:0016020; C:membrane; IEA.  
DR InterPro; IPR008155; A4\_APP.  
DR InterPro; IPR008154; A4\_extra.  
DR InterPro; IPR001255; Beta-APP.  
DR Pfam; PF02177; A4\_EXTRA; 1.  
DR Pfam; PF03494; Beta-APP; 1.  
DR PRINTS; PR00203; AMYLOIDA4.  
DR SMART; SM00006; A4\_EXTRA; 1.  
DR PROSITE; PS00319; A4\_EXTRA; 1.  
DR PROSITE; PS00320; A4\_INTRA; 1.  
SQ SEQUENCE 694 AA; 79228 MW; 2B03382D411162DC CRC64;

Query Match 68.0%; Score 2482.5; DB 13; Length 694;  
Best Local Similarity 67.7%; Pred. No. 9.5e-142;  
Matches 476; Conservative 98; Mismatches 98; Indels 31; Gaps 9;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGKTCTIDTK 66  
| | | : : | : | | | : | : | | | : | | | : | | : | | : | | | |  
Db 9 LLLMLTTLSLAIEVPSDDSVGLLAEPQVAMFCGKLNMHINVQSGKWEPTGTGKSCISTK 68  
Qy 67 EGILOQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126  
| | | : | | | | | : | | | | | | | | | : | | | : | | | : | | | | | | | |  
Db 69 EGILKYCQEVYPDLQITNVVEANQPVSIQNWCKMGRRQCRSHTHIVVPYRCLVGEFVSDA 128  
Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186  
| | | | | | | | | | | : | | : | | | | | | : | : | | | | | | | | : | | | | |  
Db 129 LLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVC 188  
Qy 187 CPLAEESDNVDSADAEEDSDVWWGGADTDYADGS--EDKVV-----EVAEEEEVAEVEE 239  
| | : | : | : | | : | | : | | | | | : | | | : | | : | | : | |  
Db 189 CPMEEQKD-LDSEEQEEANSVWWGGAETEYTDASVLKEQVTAKPDPVTEDEDEDLNNEE 247

Qy	240	EEADDDDEDDGDGEVEEEAE--PYEEATERTTSIA--TTTTTTTTESVEEVVRVPTT	292
Db	248	EEVWDNDEDDGDGEDDEDEDDDEDIIDEQDTSEQTSNIAMTTTTTTTTTESIEEVVRVPTM	307
Qy	293	AASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKAD	352
Db	308	APSPADAVDRYLEAPGDMNEHMRQKAKESLEAKHREKMSEVMREWEAAERQAKNLPKAD	367
Qy	353	KKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRP	412
Db	368	KKTIIQRFQEKVESLEKEAAGERQQLVETHMARVEALLNDRRRQALESYSSLSQSDQPRP	427
Qy	413	RHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSL	472
Db	428	RQVLNLLKKYIRAEQKDRQHTLKHFEHVREVDPKKASQIRPFVMTHLRVIEERMNQSLSL	487
Qy	473	LYNVPVAEAEIQDEVDPELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELL	532
Db	488	LYKVPQVANDIQDQVAVLVQRDQAEVTQQLSSLSQSKMRVSYGNDAIMPDLDPDSTPLDNL	547
Qy	533	PVNGEFLDDLQFPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEIS	592
Db	548	PPEQD-GLGFIHP-ESFN----QANTDNHVEPVDARPIPERGLPTRP-----EIP	591
Qy	593	EVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQ	652
Db	592	KVRLDIEERHNAGYDVRDKRLMFLAEDMGSNKGAIIGLMVGGVVIATVIVITLVMLRKKQ	651
Qy	653	YTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	652	YTSIHGGVIEVDAAVTPEERHLAKMOONGYENPTYKFFEQMON	694

09I9E7

DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 FT NON\_TER 1 1  
 SQ SEQUENCE 612 AA; 69710 MW; 59A9ACBDF9C59EFF CRC64;

Query Match 63.9%; Score 2334; DB 13; Length 612;  
 Best Local Similarity 72.4%; Pred. No. 7.5e-133;  
 Matches 459; Conservative 66; Mismatches 81; Indels 28; Gaps 12;

Qy	68	GILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDAL	127
		:     :     :     :     :     :     :     :     :     :	
Db	1	GILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPYRCLVGEFVSDAL	60
Qy	128	LVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCC	187
		:     :     :     :     :     :     :     :     :	
Db	61	LVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVCC	120
Qy	188	PLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEEEAADDED	247
		: :         :    :   : :       :  :   : :	
Db	121	P-ADAGKESESAAVEEDDSDVWVGGAEDYTENSMTR--DAAAEPAV--LEDDEDADEEE	175
Qy	248	DEDGD-----EVEEEAEPEYEEATERTT-SIATTTTTTTSVEEVVRVPTTAASTPDAVD	301
		:           :  : : :      :      :	
Db	176	DEDGDGDRDEKIEEEEE--EERTQSTSALTSTTTTTTESVDEVVRVPTPSSSPDAVD	233
Qy	302	KYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQ	361
		:                          :     :     :     :	
Db	234	RYLETPADENEHAHFLKAKESLETKHRERMSQVMREWEAAERQAKSLPRNDKKAVIQHFQ	293
Qy	362	EKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKK	421
		:    : :     :     :     :     : :       :	
Db	294	EKVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVSLLKK	353
Qy	422	YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPVAE	481
		:     :     :     :     :     :     :     :     :	
Db	354	YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSLGLLYKVPGVAD	413
Qy	482	EIQDEVDELLQKEQNYSDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLD	541
		:   :      :     :  :  :          :	
Db	414	DIQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDALMPDST---AGLELLPAEDTQGFG	469
Qy	542	DLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFR	601
		:          :                   :     : :	
Db	470	FIHP-ESFN---QPNTHNQVEPVDPARVPDLATRPVSGL---KPDDIPELRMEAEER	521
Qy	602	HDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGVV	661
		:           :      :     : :	
Db	522	HS---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIIVITLVMLRKKQYTSIHGGII	578
Qy	662	EVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
		:     :     :     :     :     :     :     :	
Db	579	EVDAAVTPEERHLSKMQQNGYENPTYKFFEQMHN	612



O8BPC7

Query Match 52.6%; Score 1923; DB 11; Length 384;  
Best Local Similarity 97.9%; Pred. No. 2.8e-108;  
Matches 376; Conservative 2; Mismatches 6; Indels 0; Gaps 0;

Qy	312	EHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEA	371
Db	1	EHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEA	60
Qy	372	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQ	431
Db	61	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHHVFNMLKKYVRAEQKDRQ	120
Qy	432	HTLKHFHEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	491
Db	121	HTLKHFHEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	180
Qy	492	QKEQNYSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHSFGA	551
Db	181	QKEQNHSDDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHPFGV	240
Qy	552	DSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQ	611



Db	133	CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV	192
Qy	177	DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAE	236
Db	193	DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD	245
Qy	237	VEE--EEA--DDDEDDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTESVE	284
Db	246	LEDFTAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNE--ENPTEPGSDGTMSDKEIT	303
Qy	285	EVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQ	344
Db	304	HDVKVPPTPLPTND--VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQ	362
Qy	345	AKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITA	404
Db	363	AKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAA	422
Qy	405	LQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE	464
Db	423	LQSDPPRPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEE	482
Qy	465	RMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTE	524
Db	483	RRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISE	525
Qy	525	TKTTVELLPVNGEFLDDLQPWHSFGADSVANTENEVEPVDARPAADRGL-----	575
Db	526	TPVDVR--VSSEES-EEIPPFHPF--HPFPALPENEGSGVGEQ---DGGLIGAEKVIN	576
Qy	576	-TTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGG	634
Db	577	SKNKVDENMVIDETLDVKEMIFNAE--RVGGLEERESVGPLREDFSLSSSALIGLLVIA	634
Qy	635	VVIATVIFITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQ	694
Db	635	VAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTYKYLEQMQ	694

Search completed: July 26, 2004, 12:46:36  
Job time : 37.3333 secs

GenCore version 5.1.6  
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OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:28 ; Search time 9 Seconds  
(without alignments)  
4032.544 Million cell updates/sec

Title: US-09-806-194A-20  
Perfect score: 3653  
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SwissProt\_42:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query Match	Length			
1	3585.5	98.2	770	1	A4_HUMAN	P05067 h amyloid b
2	3585.5	98.2	770	1	A4_MACFA	P53601 m amyloid b
3	3579	98.0	751	1	A4_SAISC	Q95241 s amyloid b
4	3530.5	96.6	770	1	A4_PIG	P79307 s amyloid b
5	3517.5	96.3	770	1	A4_CAVPO	Q60495 c amyloid b
6	3488.5	95.5	770	1	A4_MOUSE	P12023 m amyloid b
7	3488.5	95.5	770	1	A4_RAT	P08592 r amyloid b
8	2568	70.3	780	1	A4_TETFL	O73683 tetraodon f
9	2443.5	66.9	737	1	A4_FUGRU	O93279 fugu rubrip
10	1730	47.4	695	1	APP2_MOUSE	Q06335 mus musculu
11	1723	47.2	763	1	APP2_HUMAN	Q06481 homo sapien
12	1711	46.8	765	1	APP2_RAT	P15943 rattus norv
13	1185	32.4	650	1	APP1_HUMAN	P51693 homo sapien
14	1180	32.3	653	1	APP1_MOUSE	Q03157 mus musculu
15	816.5	22.4	686	1	A4_CAEEL	Q10651 caenorhabdi
16	755.5	20.7	887	1	A4_DROME	P14599 drosophila
17	287	7.9	59	1	A4_BOVIN	Q28053 bos taurus

18	283	7.7	58	1	A4_RABIT	Q28748	oryctolagus
19	283	7.7	58	1	A4_SHEEP	Q28757	ovis aries
20	282	7.7	58	1	A4_CANFA	Q28280	canis famil
21	278	7.6	57	1	A4_URSMA	Q29149	ursus marit
22	185.5	5.1	407	1	IE68_HSVSA	Q01042	herpesvirus
23	180.5	4.9	993	1	SCP1_MOUSE	Q62209	mus musculu
24	176	4.8	2004	1	MYS3_HUMAN	Q92794	homo sapien
25	175.5	4.8	802	1	NAB3_YEAST	P38996	saccharomyc
26	173.5	4.7	793	1	CALD_HUMAN	Q05682	homo sapien
27	172	4.7	771	1	CALD_CHICK	P12957	gallus gall
28	172	4.7	1498	1	GOA3_HUMAN	Q08378	homo sapien
29	169.5	4.6	297	1	TRT2_HUMAN	P45379	homo sapien
30	169.5	4.6	721	1	YCF2_OENPI	P31568	oenothera p
31	168.5	4.6	1875	1	MLP1_YEAST	Q02455	saccharomyc
32	168	4.6	1240	1	YNJ1_YEAST	P53935	saccharomyc
33	167.5	4.6	1976	1	MYHA_HUMAN	P35580	homo sapien
34	166.5	4.6	816	1	YG3A_YEAST	P53278	saccharomyc
35	166.5	4.6	1976	1	MYHA_RAT	Q9jlt0	rattus norv
36	164.5	4.5	1447	1	GOA3_MOUSE	P55937	mus musculu
37	163.5	4.5	681	1	MP10_HUMAN	O00566	homo sapien
38	162.5	4.4	712	1	NUCL_RAT	P13383	rattus norv
39	162	4.4	2017	1	MYSN_DROME	Q99323	drosophila
40	160.5	4.4	1976	1	MYHA_BOVIN	Q27991	bos taurus
41	160	4.4	694	1	NUCL_CHICK	P15771	gallus gall
42	159.5	4.4	1955	1	PUMA_PARUN	O61308	parascaris
43	158	4.3	301	1	TRT2_CHICK	P02642	gallus gall
44	157.5	4.3	706	1	NUCL_HUMAN	P19338	homo sapien
45	156.5	4.3	5596	1	MDN1_HUMAN	Q9nu22	homo sapien

# ALIGNMENTS

## RESULT 1

### A4\_HUMAN

ID A4\_HUMAN STANDARD; PRT; 770 AA.

AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;

AC Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;

DT 13-AUG-1987 (Rel. 05, Created)

DT 01-NOV-1991 (Rel. 20, Last sequence update)

DT 15-MAR-2004 (Rel. 43, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease

DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-

DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42

DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);

DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)

DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-

DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)

DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)

DE (Amyloid intracellular domain 50) (AID(50)); C31].

GN APP OR A4 OR AD1.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI\_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87144572; PubMed=2881207;  
 RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,  
 RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;  
 RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a  
 RT cell-surface receptor.";  
 RL Nature 325:733-736(1987).  
 RN [2]

RP SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=88122639; PubMed=2893289;  
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,  
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,  
 RA Cordell B.;  
 RT "A new A4 amyloid mRNA contains a domain homologous to serine  
 RT proteinase inhibitors.";  
 RL Nature 331:525-527(1988).  
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RX MEDLINE=89128427; PubMed=2783775;  
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,  
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;  
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid  
 RT is encoded by 16 exons.";  
 RL Nucleic Acids Res. 17:517-522(1989).  
 RN [4]

RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=90236318; PubMed=2110105;  
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;  
 RT "Genomic organization of the human amyloid beta-protein precursor  
 RT gene.";  
 RL Gene 87:257-263(1990):  
 RN [5]

RP ERRATUM, AND REVISIONS.  
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;  
 RL Gene 102:291-292(1991).  
 RN [6]

RP SEQUENCE FROM N.A. (ISOFORM L-APP733).  
 RC TISSUE=Leukocyte;  
 RX MEDLINE=92268136; PubMed=1587857;  
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,  
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;  
 RT "Identification and differential expression of a novel alternative  
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in  
 RT leukocytes and brain microglial cells.";  
 RL J. Biol. Chem. 267:10804-10809(1992).  
 RN [7]

RP SEQUENCE FROM N.A. (ISOFORM APP770).  
 RX MEDLINE=97263807; PubMed=9108164;  
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,  
 RA Saito M., Tsukuni S., Sakaki Y.;  
 RT "A novel method for making nested deletions and its application for  
 RT sequencing of a 300 kb region of human APP locus.";  
 RL Nucleic Acids Res. 25:1802-1808(1997).  
 RN [8]

RP SEQUENCE FROM N.A. (ISOFORM APP639).

RC TISSUE=Brain;  
 RX MEDLINE=22744650; PubMed=12859342;  
 RA Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;  
 RT "Identification of a novel alternative splicing isoform of human  
 RT amyloid precursor protein gene, APP639.";  
 RL Eur. J. Neurosci. 18:102-108(2003).  
 RN [9]  
 RP SEQUENCE FROM N.A. (ISOFORM APP305).  
 RC TISSUE=Pancreas;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [10]  
 RP SEQUENCE OF 1-10 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89016647; PubMed=3140222;  
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;  
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)  
 RT encodes a 95-kDa polypeptide.";  
 RL Nucleic Acids Res. 16:9351-9351(1988).  
 RN [11]  
 RP ERRATUM, AND REVISIONS.  
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;  
 RL Nucleic Acids Res. 16:11402-11402(1988).  
 RN [12]  
 RP SEQUENCE OF 1-75 FROM N.A.  
 RX MEDLINE=89165870; PubMed=2538123;  
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;  
 RT "Characterization of the 5'-end region and the first two exons of the  
 RT beta-protein precursor gene.";  
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).  
 RN [13]  
 RP SEQUENCE OF 18-50.  
 RC TISSUE=Fibroblast;  
 RX MEDLINE=87250462; PubMed=3597385;  
 RA van Nostrand W.E., Cunningham D.D.;  
 RT "Purification of protease nexin II from human fibroblasts.";  
 RL J. Biol. Chem. 262:8508-8514(1987).  
 RN [14]

RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).  
 RC TISSUE=Brain;  
 RX MEDLINE=89346754; PubMed=2569763;  
 RA de Sauvage F., Octave J.N.;  
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly  
 RT secreted protein.";  
 RL Science 245:651-653(1989).  
 RN [15]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=87231971; PubMed=3035574;  
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;  
 RT "Molecular cloning and characterization of a cDNA encoding the  
 RT cerebrovascular and the neuritic plaque amyloid peptides.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).  
 RN [16]  
 RP SEQUENCE OF 286-366 FROM N.A.  
 RX MEDLINE=88122640; PubMed=2893290;  
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,  
 RA Gusella J.F., Neve R.L.;  
 RT "Protease inhibitor domain encoded by an amyloid protein precursor  
 RT mRNA associated with Alzheimer's disease.";  
 RL Nature 331:528-530(1988).  
 RN [17]  
 RP SEQUENCE OF 287-367 FROM N.A.  
 RX MEDLINE=88122641; PubMed=2893291;  
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;  
 RT "Novel precursor of Alzheimer's disease amyloid protein shows  
 RT protease inhibitory activity.";  
 RL Nature 331:530-532(1988).  
 RN [18]  
 RP SEQUENCE OF 507-770 FROM N.A.  
 RC TISSUE=Brain cortex;  
 RX MEDLINE=88124954; PubMed=2893379;  
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,  
 RA Marotta C.A.;  
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer  
 RT disease brain: coding and noncoding regions of the fetal precursor  
 RT mRNA are expressed in the cortex.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).  
 RN [19]  
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [20]  
 RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717  
 RP AND AD GLY-717.  
 RX MEDLINE=93236601; PubMed=8476439;  
 RA Denman R.B., Rosenzwaig R., Miller D.L.;  
 RT "A system for studying the effect(s) of familial Alzheimer disease  
 RT mutations on the processing of the beta-amyloid peptide precursor.";  
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).  
 RN [21]  
 RP SEQUENCE OF 656-737 FROM N.A.



RX MEDLINE=89392030; PubMed=2675837;  
RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,  
RA Little S.P.;  
RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows  
RT similarity to soybean trypsin inhibitor.";  
RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).  
RN [22]

Query Match 98.2%; Score 3585.5; DB 1; Length 770;  
Best Local Similarity 90.0%; Pred. No. 1.4e-168;  
Matches 693; Conservative 1; Mismatches 1; Indels 75; Gaps 1;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288
      |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288
Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLKTTQEPLARD 360

Qy    289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 345
      :|||
Db    361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 420

Qy    346 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL 405
      |||
Db    421 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL 480

Qy    406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
      |||
Db    481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540

Qy    466 MNQSLSLLYNVPAAVAEEIQDEVDLLQKEQNYSDDLANMISEPRISYGNDALMPSLTET 525
      |||
Db    541 MNQSLSLLYNVPAAVAEEIQDEVDLLQKEQNYSDDLANMISEPRISYGNDALMPSLTET 600

Qy    526 KTTVELLPVNGEFSDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 585
      |||
Db    601 KTTVELLPVNGEFSDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 660

Qy    586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645
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Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIAIVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

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## RESULT 2

### A4\_MACFA

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ID      A4_MACFA          STANDARD;          PRT;          770 AA.
AC      P53601; Q95KN7;
DT      01-OCT-1996 (Rel. 34, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
GN      APP.
OS      Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC      Cercopithecinae; Macaca.
OX      NCBI_TaxID=9541;
RN      [1]
RP      SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC      TISSUE=Cerebellum;
RX      MEDLINE=91273117; PubMed=1905108;
RA      Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT      "Homology of the amyloid beta protein precursor in monkey and human
RT      supports a primate model for beta amyloidosis in Alzheimer's
RT      disease.";
RL      Am. J. Pathol. 138:1423-1435(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in
CC      cell mobility and transcription regulation through protein-protein
CC      interactions (By similarity). Can promote transcription activation
CC      through binding to APBB1/Tip60 and inhibit Notch signaling through
CC      interaction with Numb (By similarity). Couples to apoptosis-
CC      inducing pathways such as those mediated by G(0) and JIP (By
CC      similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC      Acts as a kinesin I membrane receptor, mediating the axonal
CC      transport of beta-secretase and presenilin 1 (By similarity). May
CC      be involved in copper homeostasis/oxidative stress through copper
CC      ion reduction. In vitro, copper-metallated APP induces neuronal
CC      death directly or is potentiated through Cu(II)-mediated low-
CC      density lipoprotein oxidation (By similarity). Can regulate
CC      neurite outgrowth through binding to components of the
CC      extracellular matrix such as heparin and collagen I and IV (By
CC      similarity). The splice isoforms that contain the BPTI domain
CC      possess protease inhibitor activity (By similarity).
CC      -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

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CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=APP770;  
 CC IsoId=P53601-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=P53601-2; Sequence=VSP\_000010, VSP\_000011;  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells (By similarity).  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The PID domain-containing proteins which bind APP  
 CC require the YENPTY motif for full interaction. These interactions  
 CC are independent of phosphorylation on the terminal tyrosine  
 CC residue. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis (By similarity).  
 CC -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC leads to generation and extracellular release of soluble APP  
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC retention of corresponding membrane-anchored C-terminal fragments,  
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC yields P3 peptides. This is the major secretory pathway and is  
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC gamma-secretase processing of C99 releases the amyloid beta  
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC major components of amyloid plaques, and the cytotoxic C-terminal  
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
 CC results in the production of the neurotoxic C31 peptide and the  
 CC increased production of beta-amyloid peptides (By similarity).  
 CC -!- PTM: N- and O-glycosylated (By similarity).  
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC serine residues is neuron-specific. Phosphorylation can affect APP  
 CC processing, neuronal differentiation and interaction with other  
 CC proteins (By similarity).  
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC resulting in beta-amyloid-metal aggregates (By similarity).  
 CC Extracellular zinc-binding increases binding of heparin to APP and  
 CC inhibits collagen-binding (By similarity).  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
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 CC -----

DR EMBL; M58727; AAA36829.1; -.  
 DR EMBL; M58726; AAA36828.1; -.  
 DR HSSP; P05067; 1AAP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Alternative splicing; Amyloid.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.  
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 672 770 C99 (POTENTIAL).  
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 688 770 C83 (POTENTIAL).  
 FT CHAIN 688 713 P3(42) (POTENTIAL).

FT	CHAIN	688	711	P3(40) (POTENTIAL).
FT	CHAIN	712	770	GAMMA-CTF(59) (POTENTIAL).
FT	CHAIN	714	770	GAMMA-CTF(57) (POTENTIAL).
FT	CHAIN	721	770	GAMMA-CTF(50) (POTENTIAL).
FT	CHAIN	740	770	C31 (POTENTIAL).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	724	734	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	739	740	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

Query Match 98.2%; Score 3585.5; DB 1; Length 770;  
 Best Local Similarity 90.0%; Pred. No. 1.4e-168;  
 Matches 693; Conservative 1; Mismatches 1; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240

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      |||
Db      181 GVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAEEEE 240
Qy      241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR----- 288
      |||
Db      241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVREVCSEAETGPC 300
Qy      289 ----- 288
Db      301 RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLRKTTREPLTRD 360
Qy      289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 345
      :|||
Db      361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 420
Qy      346 KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRRLALENYITAL 405
      |||
Db      421 KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRRLALENYITAL 480
Qy      406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
      |||
Db      481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540
Qy      466 MNQSLSLLYNVPAAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTET 525
      |||
Db      541 MNQSLSLLYNVPAAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTET 600
Qy      526 KTTVELLPVNGEFLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 585
      |||
Db      601 KTTVELLPVNGEFLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 660
Qy      586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645
      |||
Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      |||
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

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# RESULT 3

A4\_SAISC

ID A4\_SAISC STANDARD; PRT; 751 AA.

AC Q95241;

DT 15-DEC-1998 (Rel. 37, Created)

DT 15-DEC-1998 (Rel. 37, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
 DE protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble  
 DE APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);  
 DE Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-  
 DE CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)  
 DE (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-  
 DE secretase C-terminal fragment 50); C31].

GN APP.

OS Saimiri sciureus (Common squirrel monkey).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.  
 OX NCBI\_TaxID=9521;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Kidney, and Liver;  
 RX MEDLINE=96108492; PubMed=8532114;  
 RA Levy E., Amorim A., Frangione B., Walker L.C.;  
 RT "Beta-amyloid precursor protein gene in squirrel monkeys with  
 RT cerebral amyloid angiopathy.";  
 RL Neurobiol. Aging 16:805-808(1995).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP (By  
 CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).  
 CC Acts as a kinesin I membrane receptor, mediating the axonal  
 CC transport of beta-secretase and presenilin 1 (By similarity). May  
 CC be involved in copper homeostasis/oxidative stress through copper  
 CC ion reduction. In vitro, copper-metallated APP induces neuronal  
 CC death directly or is potentiated through Cu(II)-mediated low-  
 CC density lipoprotein oxidation (By similarity). Can regulate  
 CC neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete  
 CC maturation occurs (O-glycosylated and sulfated). After alpha-  
 CC secretase cleavage, soluble APP is released into the extracellular  
 CC space and the C-terminal is internalized to endosomes and  
 CC lysosomes. Some APP accumulates in secretory transport vesicles  
 CC leaving the late Golgi compartment and returns to the cell  
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm  
 CC and nuclei of neurons (By similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;

CC           Comment=Additional isoforms seem to exist;  
 CC           Name=APP770;  
 CC           IsoId=Q95241-1; Sequence=Displayed;  
 CC           Name=APP695;  
 CC           IsoId=Q95241-2; Sequence=Not described;  
 CC    -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC           sorting of membrane proteins to the basolateral surface of  
 CC           epithelial cells (By similarity).  
 CC    -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC           phosphorylated proteins is required for the specific binding of  
 CC           the PID domain. However additional amino acids either N- or C-  
 CC           terminal to the NPXY motif are often required for complete  
 CC           interaction. The PID domain-containing proteins which bind APP  
 CC           require the YENPTY motif for full interaction. These interactions  
 CC           are independent of phosphorylation on the terminal tyrosine  
 CC           residue. The NPXY site is also involved in clathrin-mediated  
 CC           endocytosis (By similarity).  
 CC    -!- PTM: Proteolytically processed under normal cellular conditions.  
 CC           Cleavage by alpha-secretase or alternatively by beta-secretase  
 CC           leads to generation and extracellular release of soluble APP  
 CC           peptides, S-APP-alpha and S-APP-beta, respectively, and the  
 CC           retention of corresponding membrane-anchored C-terminal fragments,  
 CC           C83 and C99. Subsequent processing of C83 by gamma-secretase  
 CC           yields P3 peptides. This is the major secretory pathway and is  
 CC           nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
 CC           gamma-secretase processing of C99 releases the amyloid beta  
 CC           proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
 CC           major components of amyloid plaques, and the cytotoxic C-terminal  
 CC           fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
 CC           similarity).  
 CC    -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
 CC           (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9  
 CC           results in the production of the neurotoxic C31 peptide and the  
 CC           increased production of beta-amyloid peptides (By similarity).  
 CC    -!- PTM: N- and O-glycosylated (By similarity).  
 CC    -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
 CC           serine residues is neuron-specific. Phosphorylation can affect APP  
 CC           processing, neuronal differentiation and interaction with other  
 CC           proteins (By similarity).  
 CC    -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
 CC           zinc, can induce histidine-bridging between beta-amyloid molecules  
 CC           resulting in beta-amyloid-metal aggregates (By similarity).  
 CC           Extracellular zinc-binding increases binding of heparin to APP and  
 CC           inhibits collagen-binding (By similarity).  
 CC    -!- SIMILARITY: Belongs to the APP family.  
 CC    -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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 CC    This SWISS-PROT entry is copyright. It is produced through a collaboration  
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 CC    -----

DR    EMBL; S81024; AAD14347.1; -.  
 DR    HSSP; P05067; 1AAP.



DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;  
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;  
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;  
 KW Proteoglycan; Amyloid; Alternative splicing.  
 FT SIGNAL 1 17 BY SIMILARITY.  
 FT CHAIN 18 751 A4 PROTEIN.  
 FT CHAIN 18 668 SOLUBLE APP-ALPHA (POTENTIAL).  
 FT CHAIN 18 652 SOLUBLE APP-BETA (POTENTIAL).  
 FT CHAIN 653 751 C99 (POTENTIAL).  
 FT CHAIN 653 694 BETA-AMYLOID PROTEIN 42 (POTENTIAL).  
 FT CHAIN 653 692 BETA-AMYLOID PROTEIN 40 (POTENTIAL).  
 FT CHAIN 669 751 C83 (POTENTIAL).  
 FT CHAIN 669 694 P3(42) (POTENTIAL).  
 FT CHAIN 669 692 P3(40) (POTENTIAL).  
 FT CHAIN 693 751 GAMMA-CTF(59) (POTENTIAL).  
 FT CHAIN 695 751 GAMMA-CTF(57) (POTENTIAL).  
 FT CHAIN 702 751 GAMMA-CTF(50) (POTENTIAL).  
 FT CHAIN 721 751 C31 (POTENTIAL).  
 FT DOMAIN 18 680 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 681 704 POTENTIAL.  
 FT DOMAIN 705 751 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 181 188 ZINC-BINDING (BY SIMILARITY).  
 FT DOMAIN 291 341 BPTI/KUNITZ INHIBITOR.  
 FT DOMAIN 316 344 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 363 428 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 504 521 COLLAGEN-BINDING (BY SIMILARITY).  
 FT DOMAIN 713 732 INTERACTION WITH G(O)-ALPHA  
 FT (BY SIMILARITY).  
 FT DOMAIN 230 260 ASP/GLU-RICH (ACIDIC).  
 FT DOMAIN 274 280 POLY-THR.  
 FT SITE 144 144 REQUIRED FOR COPPER(II) REDUCTION  
 FT (BY SIMILARITY).  
 FT ACT\_SITE 301 302 REACTIVE BOND.  
 FT SITE 652 653 CLEAVAGE (BY BETA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 653 654 CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).  
 FT SITE 668 669 CLEAVAGE (BY ALPHA-SECRETASE)  
 FT (BY SIMILARITY).  
 FT SITE 685 685 INVOLVED IN FREE RADICAL PROPAGATION  
 FT (BY SIMILARITY).

FT	SITE	687	687	INVOLVED IN OXIDATIVE REACTIONS (BY SIMILARITY).
FT	SITE	692	693	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1) (BY SIMILARITY).
FT	SITE	694	695	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2) (BY SIMILARITY).
FT	SITE	701	702	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3) (BY SIMILARITY).
FT	SITE	705	715	BASOLATERAL SORTING SIGNAL (BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9) (BY SIMILARITY).
FT	SITE	738	741	ENDOCYTOSIS SIGNAL.
FT	SITE	740	743	NPXY MOTIF.

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRDRKQCKTHPHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDHVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDVEVEEEAEPEYEEATERTTSIATTTTTTTTESVVEEVR-----	288
Db	241	EADDDDEDEDGDVEVEEEAEPEYEEATERTTSIATTTTTTTTESVVEEVREVCSEQAETGPC	300
Qy	289	-----VPTTAASTPDAVDKYL	304
Db	301	RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVIPTTAASTPDAVDKYL	360
Qy	305	ETPGDENEHAFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKV	364
Db	361	ETPGDENEHAFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKV	420
Qy	365	ESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLKKYVR	424
Db	421	ESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLKKYVR	480
Qy	425	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQ	484
Db	481	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQ	540
Qy	485	DEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLSDDLQ	544

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Db      541 DEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQ 600
Qy      545 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDS 604
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDS 660
Qy      605 GYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGVEVD 664
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 GYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVD 720
Qy      665 AAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        ||||||||||||||||||||||||||||||||
Db      721 AAVTPEERHLSKMQQNGYENPTYKFFEQMQN 751

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#### RESULT 4

##### A4\_PIG

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ID      A4_PIG          STANDARD;          PRT;    770 AA.
AC      P79307; Q29023; Q9TUI0;
DT      01-NOV-1997 (Rel. 35, Created)
DT      10-OCT-2003 (Rel. 42, Last sequence update)
DT      10-OCT-2003 (Rel. 42, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
OS      Sus scrofa (Pig).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX      NCBI_TaxID=9823;
RN      [1]
RP      SEQUENCE FROM N.A.
RA      Kimura A., Takahashi T.;
RT      "Amyloid precursor protein 770.";
RL      Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN      [2]
RP      SEQUENCE OF 1-136 FROM N.A.
RC      TISSUE=Small intestine;
RA      Winteroe A.K., Fredholm M.;
RT      "Evaluation and characterization of a porcine small intestine cDNA
RT      library.";
RL      Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      SEQUENCE OF 667-723 FROM N.A.
RC      TISSUE=Brain;
RX      MEDLINE=92017079; PubMed=1656157;
RA      Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT      "Conservation of the sequence of the Alzheimer's disease amyloid
RT      peptide in dog, polar bear and five other mammals by cross-species
RT      polymerase chain reaction analysis.";
RL      Brain Res. Mol. Brain Res. 10:299-305(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in

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cell mobility and transcription regulation through protein-protein interactions (By similarity). Can promote transcription activation through binding to APBB1/Tip60 and inhibit Notch signaling through interaction with Numb (By similarity). Couples to apoptosis-inducing pathways such as those mediated by G(O) and JIP (By similarity). Inhibits G(O) alpha ATPase activity (By similarity). Acts as a kinesin I membrane receptor, mediating the axonal transport of beta-secretase and presenilin 1 (By similarity). May be involved in copper homeostasis/oxidative stress through copper ion reduction (By similarity). In vitro, copper-metallated APP induces neuronal death directly or is potentiated through Cu(II)-mediated low-density lipoprotein oxidation (By similarity). Can regulate neurite outgrowth through binding to components of the extracellular matrix such as heparin and collagen I and IV (By similarity).

-!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators with metal-reducing activity. Bind transient metals such as copper, zinc and iron (By similarity).

-!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

-!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the

CC retention of corresponding membrane-anchored C-terminal fragments,  
CC C83 and C99. Subsequent processing of C83 by gamma-secretase  
CC yields P3 peptides. This is the major secretory pathway and is  
CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated  
CC gamma-secretase processing of C99 releases the amyloid beta  
CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),  
CC major components of amyloid plaques, and the cytotoxic C-terminal  
CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By  
CC similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis  
CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9  
CC results in the production of the neurotoxic C31 peptide and the  
CC increased production of beta-amyloid peptides (By similarity).

CC -!- PTM: N- and O-glycosylated (By similarity).

CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and  
CC serine residues is neuron-specific. Phosphorylation can affect APP  
CC processing, neuronal differentiation and interaction with other  
CC proteins (By similarity).

CC -!- PTM: Extracellular binding and reduction of copper, results in a  
CC corresponding oxidation of Cys-144 and Cys-158, and the formation  
CC of a disulfide bond (By similarity).

CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and  
CC zinc, can induce histidine-bridging between beta-amyloid molecules  
CC resulting in beta-amyloid-metal aggregates (By similarity).  
CC Extracellular zinc-binding increases binding of heparin to APP and  
CC inhibits collagen-binding (By similarity).

CC -!- SIMILARITY: Belongs to the APP family.

CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
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CC -----

DR EMBL; AB032550; BAA84580.1; -.

DR EMBL; Z84022; CAB06313.1; -.

DR EMBL; X56127; CAA39592.1; -.

DR HSSP; P05067; 1AAP.

DR InterPro; IPR008155; A4\_APP.

DR InterPro; IPR008154; A4\_extra.

DR InterPro; IPR002223; Kunitz\_BPTI.

DR Pfam; PF02177; A4\_EXTRA; 1.

DR PRINTS; PR00203; AMYLOIDA4.

DR PRINTS; PR00759; BASICPTASE.

DR ProDom; PD000222; Kunitz\_BPTI; 1.

DR SMART; SM00006; A4\_EXTRA; 1.

DR SMART; SM00131; KU; 1.

DR PROSITE; PS00319; A4\_EXTRA; 1.

DR PROSITE; PS00320; A4\_INTRA; 1.

DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.

DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.

KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;

KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;

KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;



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Db      61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHTHIVIPYRCLVG 120
Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Qy      181 GVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||:|||||:|||||
Db      181 GVEFVCCPLAEESDNIDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVADVEEEE 240
Qy      241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288
        ||:|||||
Db      241 EAEDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300
Qy      289 ----- 288
Db      301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLLKTTQEHL PQD 360
Qy      289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQA 345
        :|||||
Db      361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQA 420
Qy      346 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITAL 405
        |||
Db      421 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITAL 480
Qy      406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
        |||
Db      481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540
Qy      466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 525
        |||
Db      541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 600
Qy      526 KTTVELLPVNGEFSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTN 585
        |||
Db      601 KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660
Qy      586 IKTEEISEVKMDAEFRHDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645
        |||
Db      661 IKTEEISEVKMDAEFRHDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 695
        |||
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 770

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# RESULT 5

## A4\_CAVPO

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ID      A4_CAVPO          STANDARD;          PRT;    770 AA.
AC      Q60495; Q60496;
DT      10-OCT-2003 (Rel. 42, Created)
DT      10-OCT-2003 (Rel. 42, Last sequence update)
DT      10-OCT-2003 (Rel. 42, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid

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DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);  
DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-  
DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].  
GN APP.  
OS *Cavia porcellus* (Guinea pig).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; *Cavia*.  
OX NCBI\_TaxID=10141;  
RN [1]  
RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.  
RC TISSUE=Brain, and Liver;  
RX MEDLINE=97236426; PubMed=9116031;  
RA Beck M., Mueller D., Bigl V.;  
RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and  
RT alternative splicing.";   
RL Biochim. Biophys. Acta 1351:17-21(1997).  
RN [2]  
RP INTERACTION OF BETA-APP40 WITH APOE.  
RX MEDLINE=98007700; PubMed=9349544;  
RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,  
RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;  
RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on  
RT cerebral capillary sequestration and blood-brain barrier transport of  
RT circulating Alzheimer's amyloid beta.";   
RL J. Neurochem. 69:1995-2004(1997).  
RN [3]  
RP PROCESSING.  
RX MEDLINE=20084499; PubMed=10619481;  
RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,  
RA Bigl V.;  
RT "Guinea-pig primary cell cultures provide a model to study expression  
RT and amyloidogenic processing of endogenous amyloid precursor  
RT protein.";   
RL Neuroscience 95:243-254(2000).  
RN [4]  
RP GAMMA-SECRETASE PROCESSING.  
RX MEDLINE=20576391; PubMed=11035007;  
RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,  
RA Ziani-Cherif C., Onstead L., Sambamurti K.;  
RT "A novel gamma -secretase assay based on detection of the putative  
RT C-terminal fragment-gamma of amyloid beta protein precursor.";   
RL J. Biol. Chem. 276:481-487(2001).  
CC -!- FUNCTION: Functions as a cell surface receptor and performs  
CC physiological functions on the surface of neurons relevant to  
CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
CC cell mobility and transcription regulation through protein-protein  
CC interactions (By similarity). Can promote transcription activation  
CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
CC interaction with Numb (By similarity). Couples to apoptosis-  
CC inducing pathways such as those mediated by G(0) and JIP (By  
CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).  
CC Acts as a kinesin I membrane receptor, mediating the axonal  
CC transport of beta-secretase and presenilin 1 (By similarity). May  
CC be involved in copper homeostasis/oxidative stress through copper  
CC ion reduction (By similarity). In vitro, copper-metallated APP  
CC induces neuronal death directly or is potentiated through Cu(II)-  
CC mediated low-density lipoprotein oxidation (By similarity). Can



CC regulate neurite outgrowth through binding to components of the  
 CC extracellular matrix such as heparin and collagen I and IV (By  
 CC similarity). The splice isoforms that contain the BPTI domain  
 CC possess protease inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins  
 CC and apolipoproteins E and J in the CSF and to HDL particles in  
 CC plasma, inhibiting metal-catalyzed oxidation of lipoproteins.  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).  
 CC Associates with microtubules in the presence of ATP and in a  
 CC kinesin-dependent manner (By similarity). Soluble Abeta40 binds  
 CC all three isoforms of APOE, in vitro and in vivo. When lipidated,  
 CC ApoE3 appears to be the preferred amyloid binding isoform, while  
 CC the apoE4 isoform-beta-APP40 complex is capable of being  
 CC transported across the blood-brain barrier.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated pits  
 CC (By similarity). During maturation, the immature APP (N-  
 CC glycosylated in the endoplasmic reticulum) moves to the Golgi  
 CC complex where complete maturation occurs (O-glycosylated and  
 CC sulfated) (By similarity). After alpha-secretase cleavage, soluble  
 CC APP is released into the extracellular space and the C-terminal is  
 CC internalized to endosomes and lysosomes (By similarity). Some APP  
 CC accumulates in secretory transport vesicles leaving the late Golgi  
 CC compartment and returns to the cell surface (By similarity). APP  
 CC sorts to the basolateral surface in epithelial cells (By  
 CC similarity).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=2;  
 CC Comment=Additional isoforms, missing exons 7,8 and 15, seem to  
 CC exist. The L-isoforms, missing exon 15, are referred to as  
 CC appicans;  
 CC Name=APP770;  
 CC IsoId=Q60495-1; Sequence=Displayed;  
 CC Name=APP695;  
 CC IsoId=Q60495-2; Sequence=VSP\_007221, VSP\_007222;  
 CC -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in  
 CC brain. The longer isoforms containing the BPTI domain are  
 CC predominantly expressed in peripheral organs such as muscle and  
 CC liver.  
 CC -!- INDUCTION: Increased levels during neuronal differentiation.  
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for  
 CC sorting of membrane proteins to the basolateral surface of  
 CC epithelial cells.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of

the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue (By similarity). The NPXY site is also involved in clathrin-mediated endocytosis.

- !- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of CTF-beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the corresponding cytotoxic C-terminal fragments (CTFs).
- !- PTM: Proteolytically cleaved by caspase-3 during neuronal apoptosis (By similarity).
- !- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to the L-APP isoforms produces the APP proteoglycan core proteins, the appicans (By similarity).
- !- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and serine residues is neuron-specific (By similarity). Phosphorylation can affect APP processing, neuronal differentiation and interaction with other proteins.
- !- PTM: Extracellular binding and reduction of copper, results in a corresponding oxidation of Cys-144 and Cys-158, and the formation of a disulfide bond (By similarity).
- !- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and zinc, can induce histidine-bridging between beta-amyloid molecules resulting in beta-amyloid-metal aggregates.
- !- SIMILARITY: Belongs to the APP family.
- !- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

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DR EMBL; X97631; CAA66230.1; -.  
 DR EMBL; X99198; CAA67589.1; -.  
 DR HSSP; P05067; 1BA4.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.



Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
 |||  
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540  
 |||  
 Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 525  
 |||  
 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 600  
 |||  
 Qy 526 KTTVELLPVNGEFSDDLQPWHSFGADSVDPANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
 |||  
 Db 601 KTTVELLPVNGEFSDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660  
 |||  
 Qy 586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645  
 |||  
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720  
 |||  
 Qy 646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 695  
 |||  
 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN 770  
 |||

# RESULT 6

## A4\_MOUSE

ID A4\_MOUSE STANDARD; PRT; 770 AA.  
 AC P12023; P97487; P97942; Q99K32;  
 DT 01-OCT-1989 (Rel. 12, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease  
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:  
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99  
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein  
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase  
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))  
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)  
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)  
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain  
 DE 50) (AID(50)); C31].  
 GN APP.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88106489; PubMed=3322280;  
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;  
 RT "Complementary DNA for the mouse homolog of the human amyloid beta  
 RT protein precursor."  
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).  
 RN [2]  
 RP REVISIONS.  
 RA Yamada T.;  
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.  
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=BALB/c; TISSUE=Brain;  
 RX MEDLINE=92096458; PubMed=1756177;  
 RA de Strooper B., van Leuven F., van den Berghe H.;  
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse  
 RT is closer related to its human homolog than previously reported.";  
 RL Biochim. Biophys. Acta 1129:141-143(1991).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC STRAIN=SAMP8; TISSUE=Hippocampus;  
 RX MEDLINE=21130647; PubMed=11235921;  
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,  
 RA Alvarez J., Morley J.E.;  
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid  
 RT precursor protein of senescence accelerated mouse (SAMP8).";  
 RL Biochem. Cell Biol. 79:57-67(2001).  
 RN [5]  
 RP SEQUENCE OF 1-19 FROM N.A.  
 RX MEDLINE=92209998; PubMed=1555768;  
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,  
 RA Sakai Y.;  
 RT "Positive and negative regulatory elements for the expression of the  
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";  
 RL Gene 112:189-195(1992).  
 RN [6]  
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).  
 RC TISSUE=Breast tumor;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length human  
 RT and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [7]  
 RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.  
 RC TISSUE=Brain, and Kidney;  
 RX MEDLINE=89149813; PubMed=2493250;  
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;  
 RT "Structure and expression of the alternatively-spliced forms of mRNA  
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein  
 RT precursor.";  
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).

RN [8]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC STRAIN=CD-1; TISSUE=Placenta;  
 RX MEDLINE=89345111; PubMed=2569710;  
 RA Fukuchi K., Martin G.M., Deeb S.S.;  
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein  
 RT precursor of *Mus domesticus*.";  
 RL Nucleic Acids Res. 17:5396-5396(1989).  
 RN [9]  
 RP SEQUENCE OF 656-737 FROM N.A.  
 RC STRAIN=129/Sv;  
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,  
 RA Loring J.F., Goate A.M.;  
 RT "Introduction of six mutations into the mouse genome using 'Hit and  
 RT Run' gene-targeting: introduction of familial Alzheimer's disease  
 RT mutations into the mouse amyloid precursor protein gene and  
 RT humanization of the A-beta fragment.";  
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.  
 RN [10]  
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.  
 RX MEDLINE=93287808; PubMed=8510506;  
 RA Sola C., Mengod G., Ghatti B., Palacios J.M., Triarhou L.C.;  
 RT "Regional distribution of the alternatively spliced isoforms of beta  
 RT APP RNA transcript in the brain of normal, heterozygous and  
 RT homozygous weaver mutant mice as revealed by in situ hybridization  
 RT histochemistry.";  
 RL Brain Res. Mol. Brain Res. 17:340-346(1993).  
 RN [11]  
 RP INTERACTION WITH KNS2.  
 RX MEDLINE=21010507; PubMed=11144355;  
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;  
 RT "Axonal transport of amyloid precursor protein is mediated by direct  
 RT binding to the kinesin light chain subunit of kinesin-I.";  
 RL Neuron 28:449-459(2000).  
 RN [12]  
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;  
 RP THR-743; TYR-757; ASN-759 AND TYR-762.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [13]  
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.  
 RX MEDLINE=22028091; PubMed=11912189;  
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;  
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins  
 RT with scaffold proteins of the JNK signaling cascade.";  
 RL J. Biol. Chem. 277:20070-20078(2002).  
 RN [14]  
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.  
 RX MEDLINE=22008109; PubMed=12011466;  
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,  
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;  
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid

RT precursor protein binds Numb and inhibits Notch signaling.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).  
 RN [15]  
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.  
 RX MEDLINE=21437805; PubMed=11553691;  
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;  
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by  
 RT gamma-secretase is rapidly degraded but distributes partially in a  
 RT nuclear fraction of neurones in culture.";  
 RL J. Neurochem. 78:1168-1178(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions. Can promote transcription activation through binding  
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction  
 CC with Numb. Couples to apoptosis-inducing pathways such as those  
 CC mediated by G(0) and JIP. Inhibits G(0) alpha ATPase activity (By  
 CC similarity). Acts as a kinesin I membrane receptor, mediating the  
 CC axonal transport of beta-secretase and presenilin 1. May be  
 CC involved in copper homeostasis/oxidative stress through copper ion  
 CC reduction. Can regulate neurite outgrowth through binding to  
 CC components of the extracellular matrix such as heparin and  
 CC collagen I and IV (By similarity). The splice isoforms that  
 CC contain the BPTI domain possess protease inhibitor activity (By  
 CC similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators  
 CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis.  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits  
 CC its serine phosphorylation. Also interacts with GPCR-like protein  
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via  
 CC BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the  
 CC MT-binding domains (By similarity). Associates with microtubules  
 CC in the presence of ATP and in a kinesin-dependent manner (By  
 CC similarity). Interacts, through a C-terminal domain, with GNAO1  
 CC (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal  
 CC neurons (By similarity). Beta-amyloid associates with HADH2 (By  
 CC similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the  
 CC endoplasmic reticulum) moves to the Golgi complex where complete

Query Match 95.5%; Score 3488.5; DB 1; Length 770;  
 Best Local Similarity 87.7%; Pred. No. 8.1e-164;  
 Matches 675; Conservative 6; Mismatches 14; Indels 75; Gaps 1;





AC P08592;  
 DT 01-AUG-1988 (Rel. 08, Created)  
 DT 01-DEC-1992 (Rel. 24, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid  
 DE protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble  
 DE APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-  
 DE amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);  
 DE C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal  
 DE fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);  
 DE Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].  
 GN APP.  
 OS Rattus norvegicus (Rat).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
 OX NCBI\_TaxID=10116;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM APP695).  
 RC TISSUE=Brain;  
 RX MEDLINE=88312583; PubMed=2900758;  
 RA Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,  
 RA Seeburg P.H.;  
 RT "Alzheimer's disease amyloidogenic glycoprotein: expression pattern  
 RT in rat brain suggests a role in cell contact.";  
 RL EMBO J. 7:1365-1370(1988).  
 RN [2]  
 RP SEQUENCE OF 289-364 FROM N.A.  
 RC TISSUE=Liver;  
 RX MEDLINE=89183625; PubMed=2648331;  
 RA Kang J., Mueller-Hill B.;  
 RT "The sequence of the two extra exons in rat preA4.";  
 RL Nucleic Acids Res. 17:2130-2130(1989).  
 RN [3]  
 RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.  
 RX MEDLINE=21443797; PubMed=11483588;  
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;  
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein  
 RT family resembling gamma-secretase-like cleavage of Notch.";  
 RL J. Biol. Chem. 276:35235-35238(2001).  
 RN [4]  
 RP ALTERNATIVE SPLICING.  
 RX MEDLINE=96187032; PubMed=8624099;  
 RA Sandbrink R., Masters C.L., Beyreuther K.;  
 RT "APP gene family. Alternative splicing generates functionally related  
 RT isoforms.";  
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).  
 RN [5]  
 RP TISSUE SPECIFICITY OF APPICAN.  
 RX MEDLINE=95263526; PubMed=7744833;  
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,  
 RA Mytilineou C., Margolis R.U., Robakis N.K.;  
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in  
 RT brain and is produced by astrocytes but not by neurons in primary  
 RT neural cultures.";  
 RL J. Biol. Chem. 270:11839-11844(1995).  
 RN [6]  
 RP TISSUE SPECIFICITY OF ISOFORMS.

RX MEDLINE=97150061; PubMed=8996834;  
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;  
 RT "Expression of the APP gene family in brain cells, brain development  
 RT and aging.";  
 RL Gerontology 43:119-131(1997).  
 RN [7]  
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND  
 RP TYR-762.  
 RX MEDLINE=99127916; PubMed=9930726;  
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,  
 RA Suzuki T., Nairn A.C., Greengard P.;  
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the  
 RT Alzheimer's amyloid precursor protein.";  
 RL J. Neurochem. 72:549-556(1999).  
 RN [8]  
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.  
 RX MEDLINE=99162676; PubMed=10024358;  
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouilliot C.,  
 RA Valenza C., Prochiantz A., Allinquant B.;  
 RT "The amyloid precursor protein interacts with Go heterotrimeric  
 RT protein within a cell compartment specialized in signal  
 RT transduction.";  
 RL J. Neurosci. 19:1717-1727(1999).  
 RN [9]  
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.  
 RX MEDLINE=95256193; PubMed=7737970;  
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;  
 RT "The chondroitin sulfate attachment site of appican is formed by  
 RT splicing out exon 15 of the amyloid precursor gene.";  
 RL J. Biol. Chem. 270:10388-10391(1995).  
 RN [10]  
 RP BETA-AMYLOID METAL-BINDING.  
 RX MEDLINE=99316162; PubMed=10386999;  
 RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,  
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,  
 RA Bush A.I.;  
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen  
 RT peroxide through metal ion reduction.";  
 RL Biochemistry 38:7609-7616(1999).  
 RN [11]  
 RP BETA-AMYLOID ZINC BINDING.  
 RX MEDLINE=99343552; PubMed=10413512;  
 RA Liu S.T., Howlett G., Barrow C.J.;  
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation  
 RT of the A beta peptide of Alzheimer's disease.";  
 RL Biochemistry 38:9373-9378(1999).  
 RN [12]  
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF  
 RP GLY-704.  
 RX MEDLINE=21956095; PubMed=11959460;  
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;  
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-  
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";  
 RL Biochim. Biophys. Acta 1586:190-198(2001).  
 RN [13]  
 RP PHOSPHORYLATION.  
 RX MEDLINE=97239592; PubMed=9085254;

RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,  
 RA Greengard P., Suzuki T.;  
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is  
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and  
 RT cultured cells.";  
 RL Mol. Med. 3:111-123(1997).  
 RN [14]  
 RP PHOSPHORYLATION ON SER-730.  
 RX MEDLINE=99262094; PubMed=10329382;  
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,  
 RA Greengard P., Nairn A.C., Suzuki T.;  
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid  
 RT precursor protein at Ser655 by a novel protein kinase.";  
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).  
 RN [15]  
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF  
 RP THR-743.  
 RX MEDLINE=99274744; PubMed=10341243;  
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,  
 RA Kirino Y., Greengard P., Suzuki T.;  
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein  
 RT during neuronal differentiation.";  
 RL J. Neurosci. 19:4421-4427(1999).  
 RN [16]  
 RP PHOSPHORYLATION ON THR-743.  
 RX MEDLINE=20396183; PubMed=10936190;  
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,  
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;  
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor  
 RT protein by cyclin-dependent kinase 5.";  
 RL J. Neurochem. 75:1085-1091(2000).  
 RN [17]  
 RP CARBOHYDRATE STRUCTURE OF APPICAN.  
 RX MEDLINE=21463085; PubMed=11479316;  
 RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,  
 RA Sugahara K., Robakis N.K.;  
 RT "Appican, the proteoglycan form of the amyloid precursor protein,  
 RT contains chondroitin sulfate E in the repeating disaccharide region  
 RT and 4-O-sulfated galactose in the linkage region.";  
 RL J. Biol. Chem. 276:37155-37160(2001).  
 CC -!- FUNCTION: Functions as a cell surface receptor and performs  
 CC physiological functions on the surface of neurons relevant to  
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in  
 CC cell mobility and transcription regulation through protein-protein  
 CC interactions (By similarity). Can promote transcription activation  
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through  
 CC interaction with Numb (By similarity). Couples to apoptosis-  
 CC inducing pathways such as those mediated by G(O) and JIP. Inhibits  
 CC G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,  
 CC mediating the axonal transport of beta-secretase and presenilin 1  
 CC (By similarity). May be involved in copper homeostasis/oxidative  
 CC stress through copper ion reduction. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I and IV (By similarity). The  
 CC splice isoforms that contain the BPTI domain possess protease  
 CC inhibitor activity (By similarity).  
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

CC with metal-reducing activity. Bind transient metals such as  
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind  
 CC only weakly transient metals and have little reducing activity due  
 CC to substitutions of transient metal chelating residues. Beta-APP42  
 CC may activate mononuclear phagocytes in the brain and elicit  
 CC inflammatory responses. Promotes both tau aggregation and TPK II-  
 CC mediated phosphorylation (By similarity).  
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the  
 CC extracellular matrix and may regulate neurite outgrowth in the  
 CC brain.  
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved  
 CC peptides, including C31, are potent enhancers of neuronal  
 CC apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB family members, the APBA  
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding  
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also  
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2  
 CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.  
 CC In vitro, it binds MAPT via the MT-binding domains (By  
 CC similarity). Associates with microtubules in the presence of ATP  
 CC and in a kinesin-dependent manner (By similarity). Interacts,  
 CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds  
 CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid  
 CC associates with HADH2 (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface  
 CC protein that rapidly becomes internalized via clathrin-coated  
 CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 95.5%; Score 3488.5; DB 1; Length 770;  
 Best Local Similarity 87.5%; Pred. No. 8.1e-164;  
 Matches 674; Conservative 8; Mismatches 13; Indels 75; Gaps 1;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60  
 ||| ||||||||| |||||||||||||||||||||:|||||||||:|||||||  
 Db 1 MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60  
 Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120  
 ||| ||||||||||||||||||||||||||||||||||||| | |||||||||  
 Db 61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG 120  
 Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 |||||||||||||||||||||||||||||||||||||||||||||||||||  
 Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180  
 Qy 181 GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240  
 |||||||||||||:||||||||||| |||||||||||||:|||||  
 Db 181 GVEFVCCPLAEESDSIDSADAEEEDSDVWWGGADTDYADGGEDKVVEVAEEEEVADVVEE 240  
 Qy 241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288  
 ||:|||| |||||||||||||||||||||||||||||||||||||  
 Db 241 EAEDDEDVEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300  
 Qy 289 ----- 288  
 Db 301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRRNFDTEEYCMVCGSVSSQSLKTTSEPLPQD 360

Qy 289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345  
 :|||||  
 Db 361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy 346 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 405  
 |||||  
 Db 421 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 480

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465  
 |||||  
 Db 481 QAVPPRPHHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540

Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRI SYGNDALMPSLTET 525  
 |||||  
 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRI SYGNDALMPSLTET 600

Qy 526 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585  
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 Db 601 KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN 660

Qy 586 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITL 645  
 |||||  
 Db 661 IKTEEISEVKMDAEFGHDSGFVHRHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720

Qy 646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
 |||||  
 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

# RESULT 8

## A4\_TETFL

ID A4\_TETFL STANDARD; PRT; 780 AA.  
 AC O73683;  
 DT 10-OCT-2003 (Rel. 42, Created)  
 DT 10-OCT-2003 (Rel. 42, Last sequence update)  
 DT 10-OCT-2003 (Rel. 42, Last annotation update)  
 DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:  
 DE Beta-amyloid protein (Beta-APP) (A-beta)].  
 GN APP.  
 OS Tetraodon fluviatilis (Puffer fish).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;  
 OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;  
 OC Tetraodontoidea; Tetraodontidae; Tetraodon.  
 OX NCBI\_TaxID=47145;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98252138; PubMed=9599080;  
 RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;  
 RT "Analysis of pufferfish homologues of the AT-rich human APP gene."  
 RL Gene 210:17-24(1998).  
 CC !- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC !- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC !- SIMILARITY: Belongs to the APP family.  
 CC !- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----  
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 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----

DR EMBL; AF018165; AAC41275.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; FALSE\_NEG.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;  
 KW Serine protease inhibitor.  
 FT SIGNAL 1 18 POTENTIAL.  
 FT CHAIN 19 780 ALZHEIMER'S DISEASE AMYLOID A4 PROTEIN  
 FT HOMOLOG.  
 FT CHAIN 682 724 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN 19 711 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 712 732 POTENTIAL.  
 FT DOMAIN 733 780 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 323 382 BPTI/KUNITZ INHIBITOR.  
 FT SITE 769 772 CLATHRIN-BINDING (BY SIMILARITY).  
 FT DISULFID 327 378 BY SIMILARITY.  
 FT DISULFID 336 361 BY SIMILARITY.  
 FT CARBOHYD 560 560 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 SQ SEQUENCE 780 AA; 88238 MW; 60071BE94520191D CRC64;

Query Match 70.3%; Score 2568; DB 1; Length 780;  
 Best Local Similarity 65.3%; Pred. No. 9.3e-119;  
 Matches 512; Conservative 71; Mismatches 95; Indels 106; Gaps 10;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTIDTK 66  
 |||:| : | |||| : |||||:||||:| : ||||:| : ||||:| ||  
 Db 8 LLLVAAASTLAAEVPTDVSMLLAEPQVAMFCGKINMHINVQSGKWEPPDSGKTSCIGTK 67  
 Qy 67 EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126  
 |||||:|||||:|||||:||||:| | :|:|||||:|||||  
 Db 68 EGILQYCQEVYPELQITNVVEANQPVSIQNWCKKGRKQCRSHMHIVVPYRCLVGEFVSDA 127  
 Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186  
 |||||:|:|||||:| :: |||||:|||||

Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRAMNLHDYGMLLPCGIDRFRGVEFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWWGGADTDYADGS-----EDKVVEVAEEE 232  
 || || :|| : : ||||| ||||| ||:| | ||| ||

Db 188 CP-AEAERDMNSTEKDADSDVWWGGADNDYSDNSMVREPEPAEQQEETRPSVVEEEEG 246

Qy 233 EVAEVEEEE-----ADDEDEDEDGDEVEEEAEPEYEEATERTTSIA 273  
 |||: :|| | |||: ||| ||: | :| | ||:|

Db 247 EVAQEDDEEEEVLDTDQDGDGEEDHEAADDEEEEDVDEIDAFGESDDVDADEPTTNVA 306

Qy 274 ---TTTTTTTSESVEEVVR----- 288  
 ||||| |||||

Db 307 MTTTTTTTTTSESVEEVVRMFCWAHADTGPCTASMPSWYFDAVDGRTMYELMYGGCGNMN 366

Qy 289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQ 333  
 || | :||| ||| ||||| ||||| ||||| |||||

Db 367 NFESEYCLSVCSVVPTDMPSSPDAVDHYLETADENEHAHFQKAKESLEAKHRERMSQ 426

Qy 334 VMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR 393  
 ||||| :||| || | ||||: ||||: ||||| ||||| :|||

Db 427 VMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEALLNDR 486

Qy 394 RRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS 453  
 ||||| :||| ||||| :||||| ||||| ||||| ||||| |||||

Db 487 RRLALENYLTALQQDPPRPRHVFSLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRP 546

Qy 454 QVMTHLRVIYERMNQSLSLLYNPAVAEEIQDEVDELLQKEQNYSDDLANMISEPRISY 513  
 ||: |||| | |||| || | ||: ||: | |||: | |||: :| :||

Db 547 QVLTHLRVIEERMNQSLGLLYKVPGVADDIQDQV-ELLQREQAEMAQQLANLQTDVVRVSY 605

Qy 514 GNDALMPSLTETKTTVELLPVNGEFLDDLQPDWH--SFGADSVPAANTENEVEPVDARPA 571  
 ||||| :|| | :| : | || | |||: ||||: ||

Db 606 GNDALMPDQELGDGQADLLP--QEDTLGGVGFVHPESFN----QLNTENQVEPVD SRPTF 659

Qy 572 DRGLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKL VFFAEDVGSNKGAI IGLM 631  
 :||: ||| :| | : ||: || | : ||||| ||||| ||||| |||||

Db 660 ERGVPTRP---VTGKSMEAVPEL RMETEDRQSTEYEVHHQKL VFFAEDVGSNKGAI IGLM 716

Qy 632 VGGVVIATVIFITLVMLKKKQYTSIHGHVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 ||||| ||||| :||||| :||||| ||||| ||||| ||||| |||||

Db 717 VGGVVIATVIVITLVMLRKKQYTSIHGHIIEVDAAVTPEERHLSKMQQNGYENPTYKFFE 776

Qy 692 QMQN 695  
 ||||

Db 777 QMQN 780

RESULT 9

A4\_FUGRU

ID A4\_FUGRU STANDARD; PRT; 737 AA.

AC 093279;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.

OS Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;  
 OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;  
 OC Tetradontoidea; Tetraodontidae; Takifugu.  
 OX NCBI\_TaxID=31033;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98252138; PubMed=9599080;  
 RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;  
 RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";  
 RL Gene 210:17-24(1998).  
 CC -!- FUNCTION: Functional neuronal receptor which couples to  
 CC intracellular signaling pathway through the GTP-binding protein  
 CC G(O) (By similarity).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -!- SIMILARITY: Belongs to the APP family.  
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
 CC -----  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 DR EMBL; AF090120; AAD13392.1; -.  
 DR HSSP; P05067; 1HZ3.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR001255; Beta-APP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF03494; Beta-APP; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; FALSE\_NEG.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;  
 KW Serine protease inhibitor.  
 FT SIGNAL 1 18 POTENTIAL.  
 FT CHAIN 19 737 ALZHEIMER'S DISEASE AMYLOID A4  
 FT PROTEIN HOMOLOG.  
 FT CHAIN 639 681 BETA-AMYLOID PROTEIN (POTENTIAL).  
 FT DOMAIN 19 668 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 669 689 POTENTIAL.  
 FT DOMAIN 690 737 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 286 344 BPTI/KUNITZ INHIBITOR.  
 FT SITE 726 729 CLATHRIN-BINDING (BY SIMILARITY).  
 FT ACT\_SITE 300 301 REACTIVE BOND.





Qy            663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695  
               |||||:|||||  
 Db            705 VDAAVTPEERHLARMQQQNGYENPTYKFFEQMQN 737

RESULT 10

APP2\_MOUSE

ID   APP2\_MOUSE        STANDARD;        PRT;    695 AA.  
 AC   Q06335;  
 DT   01-JUN-1994 (Rel. 29, Created)  
 DT   01-FEB-1996 (Rel. 33, Last sequence update)  
 DT   15-MAR-2004 (Rel. 43, Last annotation update)  
 DE   Amyloid-like protein 2 precursor (CDEI-box binding protein) (CDEBP).  
 GN   APLP2.  
 OS   Mus musculus (Mouse).  
 OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX   NCBI\_TaxID=10090;  
 RN   [1]  
 RP   SEQUENCE FROM N.A.  
 RC   TISSUE=Fetal brain;  
 RA   von der Kammer H.;  
 RL   Submitted (JUL-1994) to the EMBL/GenBank/DDBJ databases.  
 RN   [2]  
 RP   SEQUENCE OF 1-246 FROM N.A.  
 RX   MEDLINE=94032480; PubMed=8218408;  
 RA   Hanes J., von der Kammer H., Kristjansson G.I., Scheit K.H.;  
 RT   "The complete cDNA coding sequence for the mouse CDEI binding  
 RT   protein.";  
 RL   Biochim. Biophys. Acta 1216:154-156(1993).  
 RN   [3]  
 RP   SEQUENCE OF 185-695 FROM N.A.  
 RC   STRAIN=BALB/c; TISSUE=Heart;  
 RX   MEDLINE=93129193; PubMed=1482349;  
 RA   Vidal F., Blangy A., Rassoulzadegan M., Cuzin F.;  
 RT   "A murine sequence-specific DNA binding protein shows extensive local  
 RT   similarities to the amyloid precursor protein.";  
 RL   Biochem. Biophys. Res. Commun. 189:1336-1341(1992).  
 RN   [4]  
 RP   SEQUENCE OF 1-35 FROM N.A.  
 RC   STRAIN=129/Sv;  
 RX   MEDLINE=96029629; PubMed=7592716;  
 RA   von Koch C.S., Lahiri D.K., Mammen A.L., Copeland N.G.,  
 RA   Gilbert D.J., Jenkins N.A., Sisodia S.S.;  
 RT   "The mouse APLP2 gene. Chromosomal localization and promoter  
 RT   characterization.";  
 RL   J. Biol. Chem. 270:25475-25480(1995).  
 CC   -!- FUNCTION: Binds to the DNA 5'-GTCACATG-3' (CDEI box) which plays  
 CC   an important role in the early development of embryos.  
 CC   -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC   (Potential).  
 CC   -!- SIMILARITY: Belongs to the APP family.

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[illegible]

RC TISSUE=Ovary;  
 RX MEDLINE=95217334; PubMed=7702756;  
 RA von der Kammer H., Hanes J., Klaudiny J., Scheit K.H.;  
 RT "A human amyloid precursor-like protein is highly homologous to a  
 RT mouse sequence-specific DNA-binding protein.";  
 RL DNA Cell Biol. 13:1137-1143(1994).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Brain;  
 RX MEDLINE=94035131; PubMed=8220435;  
 RA Wasco W., Gurubhagavatula S., Paradis M., Romano D.M., Sisodia S.S.,  
 RA Hyman B.T., Neve R.L., Tanzi R.E.;  
 RT "Isolation and characterization of APLP2 encoding a homologue of the  
 RT Alzheimer's associated amyloid beta protein precursor.";  
 RL Nat. Genet. 5:95-99(1993).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM 3).  
 RC TISSUE=Lung;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 CC -!- FUNCTION: May play a role in the regulation of hemostasis. The  
 CC soluble form may have inhibitory properties towards coagulation  
 CC factors. May interact with cellular G-protein signaling pathways.  
 CC May bind to the DNA 5'-GTACATG-3'(CDEI box).  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear  
 CC (Potential).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=3;  
 CC Comment=Additional isoforms seem to exist;  
 CC Name=1;  
 CC IsoId=Q06481-1; Sequence=Displayed;  
 CC Name=2;  
 CC IsoId=Q06481-2; Sequence=VSP\_000018;  
 CC Name=3;  
 CC IsoId=Q06481-3; Sequence=VSP\_000019;  
 CC -!- TISSUE SPECIFICITY: In placenta, brain, heart, lung, liver, kidney  
 CC and endothelial tissues.  
 CC -!- SIMILARITY: Belongs to the APP family.

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CC      -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC      -----
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CC      -----
DR      EMBL; S60099; AAC60589.1; -.
DR      EMBL; L09209; AAA35526.1; -.
DR      EMBL; Z22572; CAA80295.1; -.
DR      EMBL; L27631; AAC41701.1; -.
DR      EMBL; BC000373; AAH00373.1; -.
DR      PIR; A49321; A49321.
DR      HSSP; P05067; 1MWP.
DR      Genew; HGNC:598; APLP2.
DR      MIM; 104776; -.
DR      GO; GO:0016021; C:integral to membrane; NAS.
DR      GO; GO:0005634; C:nucleus; IDA.
DR      GO; GO:0003677; F:DNA binding; NAS.
DR      GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; NAS.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR002223; Kunitz_BPTI.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF00014; Kunitz_BPTI; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PRINTS; PR00759; BASICPTASE.
DR      ProDom; PD000222; Kunitz_BPTI; 1.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      SMART; SM00131; KU; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
DR      PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR      PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW      Transmembrane; Signal; Alternative splicing; DNA-binding;
KW      Nuclear protein; Serine protease inhibitor.
FT      SIGNAL          1          29          POTENTIAL.
FT      CHAIN           30         763          AMYLOID-LIKE PROTEIN 2.
FT      DOMAIN          30         692          EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM        693         716          POTENTIAL.
FT      DOMAIN          717         763          CYTOPLASMIC (POTENTIAL).
FT      DOMAIN          215         280          ASP/GLU-RICH (HIGHLY ACIDIC).
FT      DOMAIN          306         364          BPTI/KUNITZ INHIBITOR.
FT      DOMAIN          215         231          POLY-GLU.
FT      ACT_SITE        320         321          REACTIVE BOND (BY SIMILARITY).
FT      DISULFID        310         360          BY SIMILARITY.
FT      DISULFID        319         343          BY SIMILARITY.
FT      DISULFID        335         356          BY SIMILARITY.
FT      VARSPLIC        308         363          Missing (in isoform 2).
FT                                     /FTId=VSP_000018.
FT      VARSPLIC        613         624          Missing (in isoform 3).
FT                                     /FTId=VSP_000019.
FT      CONFLICT        543         543          S -> I (IN REF. 1).
SQ      SEQUENCE       763 AA;  86955 MW;  CA3A7D6DDB8A28D0 CRC64;

```

Query Match 47.2%; Score 1723; DB 1; Length 763;  
Best Local Similarity 47.0%; Pred. No. 2e-77;  
Matches 371; Conservative 112; Mismatches 166; Indels 140; Gaps 20;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | | | | | | | | : | | | : | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYQCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLYQYQEMYPELQITNVMEANQVRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | : | | | : | | | : | | | : | | | : | | | : | | |
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTES 282
      : | : | | : | | | | | | | | | | | | | | | | | | | | | |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNNFESDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPK 350
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | : | | | | | : | | | | | : | | | | | : | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL 470
      | | : | : | | | | | | | | | | | | | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTVE 530
      | | | | | | | | | : | | | : | | | | : | | | | | | | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSLLDLQPVWSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTN----- 585
      | : | | | : : | | | | | | | | | | | | | | | | | | | |
Db    588 ---VSSEES-EEIPPFHPF--HPFPALPENE----DTQPELYHPM--KKGSGVGEQDGGL 635

Qy    586 IKTEE---ISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKG 625
      | | | | | : | : | | | : | : : : | | | | | | | | | |
Db    636 IGAEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEEEERESVGPLREDFSLSS 693

Qy    626 AIIGLMVGGVVIATVIFITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENP 685
      | : | | | : | | | | | : | | | | : | | | | | : | | | |
Db    694 ALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENP 753
```

Qy            686 TYKFFEQMQ 694  
              | | | : | | | |  
Db            754 TYKYLEQMQ 762

RESULT 12

APP2\_RAT

ID    APP2\_RAT            STANDARD;            PRT;    765 AA.  
AC    P15943;  
DT    01-APR-1990 (Rel. 14, Created)  
DT    01-OCT-1996 (Rel. 34, Last sequence update)  
DT    28-FEB-2003 (Rel. 41, Last annotation update)  
DE    Amyloid-like protein 2 precursor (Sperm membrane protein YWK-II).  
GN    APLP2.  
OS    Rattus norvegicus (Rat).  
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.  
OX    NCBI\_TaxID=10116;  
RN    [1]  
RP    SEQUENCE OF 1-627 FROM N.A.  
RC    STRAIN=Wistar; TISSUE=Brain, and Heart;  
RX    MEDLINE=94368849; PubMed=8086458;  
RA    Sandbrink R., Masters C.L., Beyreuther K.;  
RT    "Complete nucleotide and deduced amino acid sequence of rat amyloid  
RT    protein precursor-like protein 2 (APLP2/APPH): two amino acids length  
RT    difference to human and murine homologues.";  
RL    Biochim. Biophys. Acta 1219:167-170(1994).  
RN    [2]  
RP    SEQUENCE OF 575-765 FROM N.A.  
RC    TISSUE=Testis;  
RX    MEDLINE=90207205; PubMed=1690887;  
RA    Yan Y.C., Bai Y., Wang L.F., Miao S.Y., Koide S.S.;  
RT    "Characterization of cDNA encoding a human sperm membrane protein  
RT    related to A4 amyloid protein.";  
RL    Proc. Natl. Acad. Sci. U.S.A. 87:2405-2408(1990).  
CC    -!- SUBCELLULAR LOCATION: Type I membrane protein.  
CC    -!- ALTERNATIVE PRODUCTS:  
CC        Event=Alternative splicing; Named isoforms=4;  
CC        Name=A;  
CC        IsoId=P15943-1; Sequence=Displayed;  
CC        Name=B;  
CC        IsoId=P15943-2; Sequence=VSP\_000021;  
CC        Name=C;  
CC        IsoId=P15943-3; Sequence=VSP\_000020;  
CC        Name=D;  
CC        IsoId=P15943-4; Sequence=VSP\_000020, VSP\_000021;  
CC    -!- SIMILARITY: Belongs to the APP family.  
CC    -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.  
CC    -----  
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CC    -----



DR EMBL; X77934; CAA54906.1; -.  
 DR EMBL; M31322; AAA42352.1; -.  
 DR PIR; A35981; A35981.  
 DR PIR; S42880; S42880.  
 DR HSSP; P05067; 1MWP.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR Pfam; PF00014; Kunitz\_BPTI; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 1.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR SMART; SM00131; KU; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 DR PROSITE; PS00280; BPTI\_KUNITZ\_1; 1.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 1.  
 KW Transmembrane; Alternative splicing; Serine protease inhibitor;  
 KW Signal; Glycoprotein.  
 FT SIGNAL 1 29 POTENTIAL.  
 FT CHAIN 30 765 AMYLOID-LIKE PROTEIN 2.  
 FT DOMAIN 30 695 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 696 718 POTENTIAL.  
 FT DOMAIN 719 765 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 218 282 ASP/GLU-RICH (HIGHLY ACIDIC).  
 FT DOMAIN 308 366 BPTI/KUNITZ INHIBITOR.  
 FT ACT\_SITE 322 323 REACTIVE BOND (BY SIMILARITY).  
 FT DISULFID 312 362 BY SIMILARITY.  
 FT DISULFID 321 345 BY SIMILARITY.  
 FT DISULFID 337 358 BY SIMILARITY.  
 FT DOMAIN 218 229 POLY-GLU.  
 FT CARBOHYD 628 628 O-LINKED (GLYCOSAMINOGLYCAN) (POTENTIAL).  
 FT VARSPLIC 311 365 Missing (in isoform C and isoform D).  
 FT /FTId=VSP\_000020.  
 FT VARSPLIC 616 627 Missing (in isoform B and isoform D).  
 FT /FTId=VSP\_000021.  
 FT CONFLICT 575 577 DQF -> EFV (IN REF. 2).  
 SQ SEQUENCE 765 AA; 86882 MW; CF51FCCCE305A0CF CRC64;

Query Match 46.8%; Score 1711; DB 1; Length 765;  
 Best Local Similarity 46.1%; Pred. No. 7.9e-77;  
 Matches 363; Conservative 122; Mismatches 167; Indels 136; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56  
 | :||| || | : ||| :|||||||:||||:|:| ||: ||  
 Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74  
 Qy 57 SGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116  
 :|||:|: ||| :|||||:|||||||:||||| | :||:| :|||:| | |||:|  
 Db 75 TGTKSCLGTKEEVLYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132  
 Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176  
 ||||| ||||: |:| ||||:||| | |||| || | : |: |||||:|  
 Db 133 CLVGEFVSDVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV 192

Qy	177	DKFRGVEFVCCPLAE--ESDNVDSADAEEDDSVDVWGGADTDYA-DGSEDKVVEVAEEEE	233
Db	193	DQFHGTEYVCCPQTKVVDSDSTMSKEEEEEEEEE---DEEDYALDKSEFPTEADLEDFT	248
Qy	234	VAEVEEEEEADDEDDEDEGDEVEEEAAEPPYEE-----ATERTTSIATTTTTTTTSESVEEVV	287
Db	249	EAAADEDEDEEEEEEEEEEGEEVVEDRDYYYDSFKGDDYNEENPTEPSSDGTISDKEIAHDV	308
Qy	288	R-----VPT	291
Db	309	KAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRRNFESEDYCMVCKTMI PP	368
Qy	292	TAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKA	351
Db	369	TPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRSRMDRVKKEWEEAELQAKNLPKA	427
Qy	352	DKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPR	411
Db	428	ERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRLALENYLAALQSDPPR	487
Qy	412	PRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL	471
Db	488	PHRILQALRRYVRAENKDRDLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL	547
Qy	472	LLYNVPAVAEEIQDEVDELLOKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVEL	531
Db	548	LLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTSSISENPVDVR-	589
Qy	532	LPVNGEFLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTN-----I	586
Db	590	--VSSEES-EEIPPFHPF--HPFPSLSENE----DTQPELYHPM--KKGSGMAEQDGGLI	638
Qy	587	KTEE---ISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKG	626
Db	639	GAEKVKINSKNKMDENMVIDETLDV--KEMIFNAERVGGLEEEPPDSVGPLREDFSLSSA	696
Qy	627	IIGLMVGGVVIATVIFITLVMKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPT	686
Db	697	LIGLLVIAVAIATVIVISLVMRLKRQYGTISHGIVEVHPMLTPEERHLNKMQNHYENPT	756
Qy	687	YKFFEQQM 694	
Db	757	YKYLEQQM 764	

OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98088960; PubMed=9428684;  
 RA Paliga K., Peraus G., Kreger S., Duwrrwang U., Hesse L., Multhaup G.,  
 RA Masters C.L., Beyreuther K., Weidemann A.;  
 RT "Human amyloid precursor-like protein 1 -- cDNA cloning, ectopic  
 RT expression in COS-7 cells and identification of soluble forms in the  
 RT cerebrospinal fluid.";  
 RL Eur. J. Biochem. 250:354-363(1997).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=98180887; PubMed=9521588;  
 RA Lenkkeri U., Kestila M., Lamerdin J., McCready P., Adamson A.,  
 RA Olsen A., Tryggvason K.;  
 RT "Structure of the human amyloid-precursor-like protein gene APLP1 at  
 RT 19q13.1.";  
 RL Hum. Genet. 102:192-196(1998).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Ovary;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalón D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [4]  
 RP POSSIBLE FUNCTION, AND TISSUE SPECIFICITY.  
 RX MEDLINE=96115107; PubMed=7494461;  
 RA Kim T.-W., Wu K., Xu J.-L., McAuliffe G., Tanzi R.E., Wasco W.,  
 RA Black I.B.;  
 RT "Selective localization of amyloid precursor-like protein 1 in the  
 RT cerebral cortex postsynaptic density.";  
 RL Brain Res. Mol. Brain Res. 32:36-44(1995).  
 RN [5]  
 RP HEPARIN AND ZINC BINDING.  
 RX MEDLINE=95014513; PubMed=7929392;  
 RA Bush A.I., Pettingell W.H. Jr., de Paradis M., Tanzi R.E., Wasco W.;  
 RT "The amyloid beta-protein precursor and its mammalian homologues.  
 RT Evidence for a zinc-modulated heparin-binding superfamily.";  
 RL J. Biol. Chem. 269:26618-26621(1994).

RN [6]  
RP INTERACTION WITH APBA2.  
RX MEDLINE=99107877; PubMed=9890987;  
RA Tomita S., Ozaki T., Taru H., Oguchi S., Takeda S., Yagi Y.,  
RA Sakiyama S., Kirino Y., Suzuki T.;  
RT "Interaction of a neuron-specific protein containing PDZ domains with  
RT Alzheimer's amyloid precursor protein.";  
RL J. Biol. Chem. 274:2243-2254(1999).

RN [7]  
RP EXTRACELLULAR COPPER-BINDING.  
RX MEDLINE=22130992; PubMed=12135352;  
RA Simons A., Ruppert T., Schmidt C., Schlicksupp A., Pipkorn R.,  
RA Reed J., Masters C.L., White A.R., Cappai R., Beyreuther K.,  
RA Bayer T.A., Multhaup G.;  
RT "Evidence for a copper-binding superfamily of the amyloid precursor  
RT protein.";  
RL Biochemistry 41:9310-9320(2000).

CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
CC gamma-secretase processed fragment, ALID1, activates transcription  
CC activation through APBB1 (Fe65) binding (By similarity). Couples  
CC to JIP signal transduction through C-terminal binding. May  
CC interact with cellular G-protein signaling pathways. Can regulate  
CC neurite outgrowth through binding to components of the  
CC extracellular matrix such as heparin and collagen I.  
CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
CC neuronal apoptosis (By similarity).  
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
CC cytoplasmic proteins, including APBB and APBA family members,  
CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
CC serine phosphorylation (By similarity).  
CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
CC processed in the Golgi complex.  
CC -!- TISSUE SPECIFICITY: Expressed in the cerebral cortex where it is  
CC localized to the postsynaptic density (PSD).  
CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
CC phosphorylated proteins is required for the specific binding of  
CC the PID domain. However additional amino acids either N- or C-  
CC terminal to the NPXY motif are often required for complete  
CC interaction. The NPXY site is also involved in clathrin-mediated  
CC endocytosis.  
CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
CC apoptosis. Cleaved, in vitro, at Asp-620 by caspase-3 (By  
CC similarity).  
CC -!- PTM: N- and O-glycosylated.  
CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
CC Zinc-binding increases heparin binding. No Cu(II) reducing  
CC activity with copper-binding.  
CC -!- SIMILARITY: Belongs to the APP family.

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CC -----

DR EMBL; U48437; AAB96331.1; -.  
 DR EMBL; AD000864; AAB50173.1; -.  
 DR EMBL; BC012889; AAH12889.1; -.  
 DR HSSP; P05067; 1MWP.  
 DR Genew; HGNC:597; APLP1.  
 DR MIM; 104775; -.  
 DR GO; GO:0005604; C:basement membrane; TAS.  
 DR GO; GO:0007397; P:histogenesis and organogenesis; TAS.  
 DR GO; GO:0007399; P:neurogenesis; TAS.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Coated pits; Neurone;  
 KW Heparin-binding; Metal-binding; Copper; Zinc; Signal; Transmembrane;  
 KW Glycoprotein.  
 FT SIGNAL 1 38 POTENTIAL.  
 FT CHAIN 39 650 AMYLOID-LIKE PROTEIN 1.  
 FT CHAIN 621 650 C30 (BY SIMILARITY).  
 FT DOMAIN 39 580 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 581 603 POTENTIAL.  
 FT DOMAIN 604 650 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 158 178 COPPER-BINDING (BY SIMILARITY).  
 FT DOMAIN 204 211 ZINC-BINDING.  
 FT DOMAIN 310 342 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 410 441 HEPARIN-BINDING (BY SIMILARITY).  
 FT DOMAIN 442 459 COLLAGEN-BINDING (BY SIMILARITY).  
 FT DOMAIN 640 643 CLATHRIN-BINDING (POTENTIAL).  
 FT DOMAIN 241 247 POLY-GLU.  
 FT DOMAIN 264 268 POLY-GLU.  
 FT SITE 167 167 REQUIRED FOR COPPER(II) REDUCTION (BY  
 FT SIMILARITY).  
 FT SITE 604 615 BASOLATERAL SORTING SIGNAL (BY  
 FT SIMILARITY).  
 FT SITE 620 621 CLEAVAGE (BY CASPASE-3) (BY SIMILARITY).  
 FT SITE 638 641 ENDOCYTOSIS SIGNAL (BY SIMILARITY).  
 FT SITE 640 643 NPXY MOTIF.  
 FT CARBOHYD 337 337 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 461 461 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 551 551 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CONFLICT 48 48 A -> P (IN REF. 1).  
 SQ SEQUENCE 650 AA; 72176 MW; B95F0F4D1C5CBAC7 CRC64;

Query Match 32.4%; Score 1185; DB 1; Length 650;  
 Best Local Similarity 38.7%; Pred. No. 3.6e-51;  
 Matches 271; Conservative 115; Mismatches 231; Indels 84; Gaps 16;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60  
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 Db 23 LLPLLLLLLLRAQPAIGSLAGGSPGAAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRSR 82  
 Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCLV 119  
 |: : :|:|:|:|:|:| | :| | : :| | | ||| |:|:|:|:|  
 Db 83 RCLRDPQRVLEYCRQMPYELQIARVEQATQAIPMERWCGGSRSGSCAHPHHQVVPFRCLP 142

Qy 120 GEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKF 179  
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 Db 143 GEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQEACSSQGLILHGSGLMPCGSDRF 202

Qy 180 RGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEE 239  
 ||||:|||| | | | | | | | | | | | | | | | | | |  
 Db 203 RGVEYVCCPPPGTPD--PSGTAVGDPSTRSW-----PPGSR---VEGADEEE----EE 246

Qy 240 EEADDDDEDD--EDGDEVEEEAEEPVEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP 297  
 | | | : : ||| | : | : | | | | | |  
 Db 247 ESFPQPVDYFVEPPQAEEE--EETVPPSSHTLAVVGKVTPTPR-----PT----- 291

Qy 298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357  
 | | | | ||: :|| | :|| | | : :||| | | : | :||| | | :||:  
 Db 292 DGVDIYFGMPGEI SEHEGFLRAKMDLEERRMRQINEVMREWAMADNQSKNLPKADRQALN 351

Qy 358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417  
 :||| :|||: : |||:|||| | | | :||| | | | : ||| | | : |  
 Db 352 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQADPPQAERVLL 411

Qy 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477  
 | : : | | | | : : | | | : | | | | | | | | | | | | | | | | | |  
 Db 412 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRQVHTLQVIEERVNQSLGLLDQNP 471

Qy 478 AVAAEQDEVDLLQKEQNYSDDVLNMISEPRISYGNLMPSLTETKTTVELLPVNGE 537  
 :|:|: : : ||| | | | | | | | | | | | | | | | | |  
 Db 472 HLAQELRPQIQELLHSEH-----LGPSELEA-----PAPGG 502

Qy 538 FSLD--DLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVK 595  
 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |  
 Db 503 SSEDKGGQLQPPDS--KDDTPM-----TLPKGSTEQDAASPEKEKMNPLEQYE 547

Qy 596 MDAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVML-KKK 651  
 | : | | | : | : | : | | : | : | : | : | : | : | : | : | : | |  
 Db 548 RKNVASVPRGFPFHSSEIQRDELAPAGTGVSRSAVSGLLIMGAGGSLIVLSMLLLRRKK 607

Qy 652 QYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692  
 | : | | | | | : | | | : | : | : | | | | | : | : | :  
 Db 608 PYGAISHGVVEVDPMILTLEEQLRELQRHGYENPTYRFL 648

# RESULT 14

## APP1\_MOUSE

ID APP1\_MOUSE STANDARD; PRT; 653 AA.  
 AC Q03157; Q8VC38;  
 DT 01-OCT-1993 (Rel. 27, Created)  
 DT 01-OCT-1993 (Rel. 27, Last sequence update)  
 DT 15-MAR-2004 (Rel. 43, Last annotation update)  
 DE Amyloid-like protein 1 precursor (APLP) (APLP-1) [Contains: C30].  
 GN APLP1.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.

RC TISSUE=Brain;  
 RX MEDLINE=93066322; PubMed=1279693;  
 RA Wasco W., Bupp K., Magendantz M., Gusella J.F., Tanzi R.E.,  
 RA Solomon F.;  
 RT "Identification of a mouse brain cDNA that encodes a protein related  
 RT to the Alzheimer disease-associated amyloid beta protein precursor.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 89:10758-10762(1992).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE=Retina;  
 RX MEDLINE=22388257; PubMed=12477932;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length  
 RT human and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [3]  
 RP COLLAGEN-BINDING.  
 RX MEDLINE=96139497; PubMed=8576160;  
 RA Behr D., Hesse L., Masters C.L., Multhaup G.;  
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and  
 RT mapping of the binding sites on APP and collagen type I.";  
 RL J. Biol. Chem. 271:1613-1620(1996).  
 RN [4]  
 RP INTERACTION WITH DAB1.  
 RX MEDLINE=99389880; PubMed=10460257;  
 RA Homayouni R., Rice D.S., Sheldon M., Curran T.;  
 RT "Disabled-1 binds to the cytoplasmic domain of amyloid precursor-like  
 RT protein 1.";  
 RL J. Neurosci. 19:7507-7515(1999).  
 RN [5]  
 RP INTERACTION WITH MAPK8IP1.  
 RX MEDLINE=21408156; PubMed=11517249;  
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,  
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,  
 RA Kyriakis J.M., Nishimoto I.;  
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1  
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";  
 RL J. Neurosci. 21:6597-6607(2001).  
 RN [6]  
 RP GAMMA-SECRETASE PROCESSING, INTERACTION WITH APBB1, AND MUTAGENESIS OF  
 RP TYR-641.

RX MEDLINE=22313598; PubMed=12228233;  
 RA Scheinfeld M.H., Gherzi E., Laky K., Fowlkes B.J., D'Adamio L.;  
 RT "Processing of beta-amyloid precursor-like protein-1 and -2 by gamma-  
 RT secretase regulates transcription.";  
 RL J. Biol. Chem. 277:44195-44201(2002).  
 CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal  
 CC gamma-secretase processed fragment, ALID1, activates transcription  
 CC activation through APBB1 (Fe65) binding. Couples to JIP signal  
 CC transduction through C-terminal binding. May interact with  
 CC cellular G-protein signaling pathways. Can regulate neurite  
 CC outgrowth through binding to components of the extracellular  
 CC matrix such as heparin and collagen I.  
 CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of  
 CC neuronal apoptosis (By similarity).  
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several  
 CC cytoplasmic proteins, including APBB and APBA family members,  
 CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its  
 CC serine phosphorylation.  
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally  
 CC processed in the Golgi complex.  
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-  
 CC phosphorylated proteins is required for the specific binding of  
 CC the PID domain. However additional amino acids either N- or C-  
 CC terminal to the NPXY motif are often required for complete  
 CC interaction. The NPXY site is also involved in clathrin-mediated  
 CC endocytosis.  
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal  
 CC apoptosis. Cleaved, in vitro, at Asp-623 by caspase-3 (By  
 CC similarity).  
 CC -!- PTM: N- and O-glycosylated.  
 CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.  
 CC Zinc-binding increases heparin binding. No Cu(II) reducing  
 CC activity with copper-binding.  
 CC -!- SIMILARITY: Belongs to the APP family.

CC -----  
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 CC -----

DR EMBL; L04538; AAA37247.1; -.  
 DR EMBL; BC021877; AAH21877.1; -.  
 DR PIR; A46362; A46362.  
 DR HSSP; P05067; 1MWP.  
 DR MGD; MGI:88046; Aplp1.  
 DR InterPro; IPR008155; A4\_APP.  
 DR InterPro; IPR008154; A4\_extra.  
 DR Pfam; PF02177; A4\_EXTRA; 1.  
 DR PRINTS; PR00203; AMYLOIDA4.  
 DR SMART; SM00006; A4\_EXTRA; 1.  
 DR PROSITE; PS00319; A4\_EXTRA; 1.  
 DR PROSITE; PS00320; A4\_INTRA; 1.  
 KW Apoptosis; Endocytosis; Cell adhesion; Coated pits; Neurone;  
 KW Heparin-binding; Metal-binding; Copper; Zinc; Signal; Transmembrane;





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      :|||  ::||:: : |||:||||  || |:|:|  |||  :: |||  ||:  |
Db      355 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:|:|:|:|:|:|:|:|:|  |||:|  |:|  ||  |||:|  |||||  ||  |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAAVDPEKAQQMRFQVQTHLQVIEERMNQSLGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      |:|:|:|  :: |||  ||  :  :  ||  :|  |  :|  |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKM 596
      |||  |:|  :|  |  :|  |  :  |  :  :  :
Db      511 ----GSLQP-----PESKDPPVTLF---KGSTDQESSSSGREKLTPLEQYEQ 551
Qy      597 DAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVML-KKKQ 652
      |:  |  |:  |  :|  |:|:|  |:|  :|  :|:|  |||
Db      552 KVNASAPRGFPFHSSDIQRDELAPSGTGVREALSGLLIMGAGGGSGLIVLSLLLLRKKKP 611
Qy      653 YTSIHGVEVDAAVTPEERHLSKMQONGYENPTYKFFEQ 692
      |:|  |||||  :|  ||:  |  :|:|:|:|:|:|  |:|
Db      612 YGTISHGVVEVDPMLTLEEQLRELQRHGYENPTYRFLEE 651

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# RESULT 15

## A4\_CAEEL

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ID      A4_CAEEL          STANDARD;          PRT;      686 AA.
AC      Q10651; Q18583; Q95ZX1;
DT      28-FEB-2003 (Rel. 41, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Beta-amyloid-like protein precursor.
GN      APL-1 OR C42D8.8.
OS      Caenorhabditis elegans.
OC      Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC      Rhabditidae; Peloderinae; Caenorhabditis.
OX      NCBI_TaxID=6239;
RN      [1]
RP      SEQUENCE OF 6-686 FROM N.A.
RC      STRAIN=Bristol N2;
RX      MEDLINE=94089766; PubMed=8265668;
RA      Daigle I., Li C.;
RT      "apl-1, a Caenorhabditis elegans gene encoding a protein related to
RT      the human beta-amyloid protein precursor.";
RL      Proc. Natl. Acad. Sci. U.S.A. 90:12045-12049(1993).
RN      [2]
RP      SEQUENCE FROM N.A.
RC      STRAIN=Bristol N2;
RA      Hallsworth K.;
RL      Submitted (MAY-1996) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      REVISIONS, AND ALTERNATIVE SPLICING.
RA      Waterston R.;
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
CC      -!- SUBCELLULAR LOCATION: Type I membrane protein (Potential).
CC      -!- ALTERNATIVE PRODUCTS:
CC      Event=Alternative splicing; Named isoforms=2;

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CC      Name=a;
CC      IsoId=Q10651-1; Sequence=Displayed;
CC      Name=b;
CC      IsoId=Q10651-2; Sequence=VSP_000017;
CC      Note=No experimental confirmation available;
CC      -!- SIMILARITY: Belongs to the APP family.
CC      -----
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CC      -----
DR      EMBL; U00240; AAC46470.1; ALT_INIT.
DR      EMBL; U56966; AAA98722.1; -.
DR      EMBL; U56966; AAK68242.1; -.
DR      PIR; T15795; T15795.
DR      HSSP; P05067; 1MWP.
DR      WormPep; C42D8.8a; CE04209.
DR      WormPep; C42D8.8b; CE27845.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
KW      Signal; Transmembrane; Amyloid; Neurogenesis; Glycoprotein;
KW      Alternative splicing.
FT      SIGNAL      1      21      POTENTIAL.
FT      CHAIN      22      686      BETA-AMYLOID-LIKE PROTEIN.
FT      DOMAIN      22      621      EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM      622      642      POTENTIAL.
FT      DOMAIN      643      686      CYTOPLASMIC (POTENTIAL).
FT      DOMAIN      205      228      ASP-RICH.
FT      DOMAIN      676      679      CLATHRIN-BINDING (POTENTIAL).
FT      CARBOHYD      84      84      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      201      201      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      249      249      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD      417      417      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      VARSPLIC      538      539      Missing (in isoform b).
FT      /FTId=VSP_000017.
SQ      SEQUENCE      686 AA; 79434 MW; A0816858FDD48608 CRC64;

Query Match      22.4%; Score 816.5; DB 1; Length 686;
Best Local Similarity 29.1%; Pred. No. 4.2e-33;
Matches 222; Conservative 110; Mismatches 275; Indels 155; Gaps 22;

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK 60
      :: || : :| | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db      6 LMIGLLIPILVA-TVYAEGSPAGSKRHEKFIPMVAFCGYRNQYM-TEEGSWKTTDDERYA 63

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || | | :| :| :| :| :| :| :| :| :| :| :| :| :| :| :| :| :| :|
Db      64 TCFSGKLDILKYCRKAYPSMNITNIVEYSHEVSISDWCREEGSPCK-WTHSVRPYHCIDG 122

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Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTN-----LHDYGMLLP 174  
 || :|| || :| | | : || | : | | : : :|| ||  
 Db 123 EFHSEALQVPHDCQFSHVNSRDQCNDYQHWKDEAGKQCKTKKSKGNKDMIVRSFAVLEPC 182

Qy 175 GIDKFRGVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEV 234  
 :| | ||||| :| : | : :  
 Db 183 ALDMFTGVEFVCCP----NDQTNKTDVQKTK----- 209

Qy 235 AEVEEEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAA 294  
 |:: ||||| | : ||::| ||  
 Db 210 ---EEDDDDDDEDDAYEDDYSEESDEKDEE----- 236

Qy 295 STPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEA-----ERQAKNLP 349  
 | : | | : ||| |::| : : ||:: : ||::| : |::|| :  
 Db 237 -EPSSQDPYFKIANWTNEHDDFKKAEMRMDEKHKRKVDKVMKEWGDLETRYNEQKAKD-P 294

Qy 350 KADKKAIVQ---HFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL- 405  
 | :| | | :|| : ||::| |:: : | ||:||||::| | :| ||  
 Db 295 KGAEKFKSQMNARFQKTVSSLEEEHKMRKEIEAVHEERVQAMLNEKKRDATHDYRQALA 354

Qy 406 -QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLVIYE 464  
 | | || :||::|| || : | : | || : | : || |  
 Db 355 THVNKPNKHSVLQSLKAYIRAEKDRMHTLNRYRHLLKADSKEAAAYKPTVIHRLRYIDL 414

Qy 465 RMNQSLSLLYNVP-----AVA--EEIQDEVDELLQKEQNYSDVLANMISEPRISY 513  
 |:| :::| : | || : : ||| : | | | :| : |  
 Db 415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE---DSELTPIIHDDFSK 470

Qy 514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLQPWHSFGADSVFANT---ENEVEP 564  
 | | :| : : :|| | : : : | | : : :  
 Db 471 NAKLDVKAPTTTAKPVKETDNAKVLPTASDSEEEADEYYEDEDDEQVKKTPDMKKKVKV 530

Qy 565 VДАРP-----AADRGLTTRPGSGLTNIKTEE-----ISEVKMDA 598  
 || :| | | | | | : : :| | : : :|  
 Db 531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDDDDDSSSSTSSEDEDEDKNIKELRVDI 590

Qy 599 E-----FRHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLK 649  
 | :|| | : | | : : : | | | :  
 Db 591 EPIIDEPASFYRHD-----KLIQSPEVERSASSVFQPYVLASAMFITAICIIAFAIT 642

Qy 650 KKQYTSIHGHVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691  
 : | :|| | ||||:: || ||||| ||:  
 Db 643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

Search completed: July 26, 2004, 12:44:43  
 Job time : 12 secs